January 2020

MICHIGAN MAC J – 8

LOCAL DETERMINATION COVERAGE (LCD)

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Covered- No ABN required if ICD-10 code(s) listed in the section specific for the test ordered.

Local Coverage Determination (LCD): Allergy Testing (L36402)

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Contractor Information

CONTRACTOR NAME	CONTRACT TYPE	CONTRACT NUMBER	JURISDICTION	STATE(S)
Wisconsin Physicians Service Insurance Corporation	MAC - Part A	05101 - MAC A	J - 05	Iowa
Wisconsin Physicians Service Insurance Corporation	MAC - Part B	05102 - MAC B	J - 05	Iowa
Wisconsin Physicians Service Insurance Corporation	MAC - Part A	05201 - MAC A	J - 05	Kansas
Wisconsin Physicians Service Insurance Corporation	MAC - Part B	05202 - MAC B	J - 05	Kansas
Wisconsin Physicians Service Insurance Corporation	MAC - Part A	05301 - MAC A	J - 05	Missouri - Entire State
Wisconsin Physicians Service Insurance Corporation	MAC - Part B	05302 - MAC B	J - 05	Missouri - Entire State
Wisconsin Physicians Service Insurance Corporation	MAC - Part A	05401 - MAC A	J - 05	Nebraska
Wisconsin Physicians Service Insurance Corporation	MAC - Part B	05402 - MAC B	J - 05	Nebraska
Wisconsin Physicians Service Insurance Corporation	MAC - Part A	05901 - MAC A	J - 05	Alabama Alaska Arizona Arkansas California - Entire State Colorado Connecticut Delaware Florida Georgia Hawaii Idaho Illinois Indiana Iowa Kansas Kentucky

CONTRACTOR NAME	CONTRACT TYPE	CONTRACT NUMBER	JURISDICTION	STATE(S)
				Louisiana Maine Maryland Massachusetts Michigan Mississippi Missouri - Entire State Montana Nebraska Nevada New Hampshire New Jersey New Mexico North Carolina North Dakota Ohio Oklahoma Oregon Pennsylvania Rhode Island South Carolina South Dakota Tennessee Texas Utah Vermont Virginia Washington West Virginia Wisconsin Wyoming
Wisconsin Physicians Service Insurance Corporation	MAC - Part A	08101 - MAC A	J - 08	Indiana
Wisconsin Physicians Service Insurance Corporation	MAC - Part B	08102 - MAC B	J - 08	Indiana
Wisconsin Physicians Service Insurance Corporation	MAC - Part A	08201 - MAC A	J - 08	Michigan
Wisconsin Physicians Service Insurance Corporation	MAC - Part B	08202 - MAC B	J - 08	Michigan

LCD Information

Document Information

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L36402

LCD Title
Allergy Testing

Proposed LCD in Comment Period
N/A

Source Proposed LCD
DL36402

AMA CPT / ADA CDT / AHA NUBC Copyright Statement

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For services performed on or after 03/18/2016

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N/A

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02/01/2016

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03/17/2016

or Laryssa Marshall at (312) 893-6814. You may also contact us at ub04@healthforum.com.

CMS National Coverage Policy

Title XVIII of the Social Security Act, Section 1833 (e) prohibits Medicare payment for any claim which lacks the necessary information to process the claim.

Title XVIII of the Social Security Act, Section 1862 (a) (1) (A) allows coverage and payment of those items or services that are considered to be *medically reasonable and necessary for the diagnosis or treatment of illness or injury or to improve the functioning of a malformed body member*.

Title XVIII of the Social Security Act, Section 1862 (a) (1) (D) excludes investigational or experimental from Medicare coverage.

Title XVIII of the Social Security Act, Section 1862 (a)(7). This section excludes routine physical examinations.

42 CFR, Section 410.20 – Physicians' Services.

42 CFR Section, 410.32 tests not ordered by the physician or other qualified non-physician provider who is treating the patient are not reasonable and necessary. (See 42 CFR 411.15(k)(1).

42 CFR, Section 410.32(b) diagnostic tests must be furnished under the appropriate level of supervision by a physician. Services furnished without the required level of supervision are not reasonable and necessary.

CMS Pub 100-02 *Medicare Benefit Policy Manual*, Chapter 15 – Covered Medical and Other Health Services, Sections
20.2 – Physician Expense for Allergy Treatment,
80.1 – Clinical Laboratory Services, and
80.6 – Requirements for Ordering and Following Orders for Diagnostic Tests.

CMS Pub 100-03 *Medicare National Coverage Determinations (NCD) Manual*, Chapter 1 – Coverage Determinations, Part 2, Sections
110.9 – Antigens Prepared for Sublingual Administration
110.11 – Food Allergy Testing and Treatment
110.12 – Challenge Ingestion Food Testing
110.13 – Cytotoxic Food Tests.

CMS Pub 100-03 *Medicare National Coverage Determinations (NCD) Manual*, Chapter 1 – Coverage Determinations, Part 4, Section 230.10 – Incontinence Control Devices.

CMS Pub 100-04 *Medicare Claims Processing Manual*, Chapter 12 – Physicians/Nonphysician Practitioners, Section 200 - Allergy Testing and Immunotherapy.
Chapter 16 – Laboratory Services, Section
40.7 – Billing for Noncovered Clinical Laboratory Tests.

Coverage Guidance

Coverage Indications, Limitations, and/or Medical Necessity

Overview:
Allergy testing is performed to determine a patient's immunologic sensitivity or reaction to particular allergens for the

purpose of identifying the cause of the allergic state. It is based on findings during a complete medical and immunologic history, and appropriate physical exam obtained by face-to-face contact with the patient.

Indications:
Allergy skin testing is a clinical procedure that is used to evaluate an immunologic response to allergenic material. It would not be expected that all patients would receive the same tests or the same number of sensitivity tests. The number and type of antigens used for testing must be chosen judiciously given the patient's presentation, history, physical findings, and clinical judgment.

To be covered by Medicare, the antigens must meet all of the following criteria:

1. Skin testing must be performed based on a complete history and physical exam,
2. Proven efficacy as demonstrated through scientifically valid peer reviewed published medical studies, and
3. Exist in the patient's environment with a reasonable probability of exposure

Allergy testing can be broadly subdivided into two methodologies:

A. In vivo testing (skin tests): this testing correlates the performance and evaluation of selective cutaneous and mucous membrane tests with the patient's history, physician examination, and other observations.

1. Percutaneous Testing (scratch, puncture, prick) and is used to evaluate immunoglobulin E (IgE) mediated hypersensitivity. Percutaneous tests require medical supervision, since there is a small but significant risk of anaphylaxis. Overall, skin testing is quick, safe, and cost-effective. It remains the test of choice in most clinical situations where immediate hypersensitivity reactions are suspected.

Percutaneous testing is the usual preferred method for allergy testing. Medicare covers percutaneous (scratch, prick or puncture) testing when IgE-mediated reactions occur with **any** of the following:

a. Inhalants.
b. Foods. (Patients present with signs and symptoms such as urticarial, angioedema, esosinophilic esophagitis, or anaphylaxis after ingestion of specific foods. Testing for food allergies in patients who present with wheezing is occasionally required.)
c. Hymenoptera (stinging insects).
d. Specific drugs (penicillins, macromolecular agents, enzymes, and egg-containing vaccines). Skin testing is unreliable with other drugs.

2. Intracutaneous/Intradermal Tests are usually performed when increased sensitivity is the main goal such as when percutaneous tests are negative and there is a strong suspicion of allergen sensitivity. Intradermal tests are injections of small amounts of antigen into the superficial layers of the skin. The usual testing program may include 2 concentrations of an extract: a weaker concentration and a stronger concentration. It would not be expected that 3 or more concentrations of one extract would be medically necessary. Medicare covers intradermal (intracutaneous) testing when IgE-mediated reactions occur to **any** of the following:

a. Inhalants.
b. Hymenoptera (stinging insects).
c. Specific drugs (penicillin's and macromolecular agents).
d. Vaccines.

3. Patch Testing is the gold standard method of identifying the cause of allergic contact dermatitis. This testing is indicated to evaluate a nonspecific dermatitis, pruritus, to differentiate allergic contact dermatitis (ACD) and irritant contact dermatitis (ICD) and determine the causative antigen. It is a diagnostic test reserved for patients with skin eruptions for which a contact allergy source is likely.

The patch test procedure can induce an eczematous reaction in miniature by applying suspect allergens to normal skin, allowing the physician to determine a specific patient allergy. Patch tests are applied to the skin on the patient's back and left in place for 48 hours. The test is interpreted after 48 hours, and typically once again at 72 or 96 hours, and the reactions are systematically scored and recorded. The patient is then informed and educated regarding specific allergies and avoidance of exposure. Avoidance of the identified allergen(s) is critical to patient improvement and resolution of the dermatitis.

Allergy patch testing is a covered procedure only when used to diagnose allergic contact dermatitis after the following exposures: dermatitis due to detergents, oils and greases, solvents, drugs and medicines in contact with skin, other chemical products, food in contact with skin, plants (except food), cosmetics, metals, rubber additives, other and unspecified. Patch tests may also be used and may be helpful when a distribution and persistence of dermatitis suggests a possible contact allergy, but the exact etiology of the dermatitis is unknown.

The clinician should recognize that contact sensitization to metals or bone cement that is used in orthopedic, cardiac, dental, and gynecological implants has been associated with both dermatitis and noncutaneous complications. These complications may include
localized pain, swelling, erythema, warmth, implant loosening, decreased range of motion, stent stenosis, and pericardial effusions in the case of cardiac implants. Patch testing to implant or device components has been recommended to help determine the etiology of the adverse reaction.

4. Photo Patch Testing uses two patches, with one of them being irradiated with ultraviolet light half way through the occlusive period. It is indicated to evaluate unique allergies resulting from light exposure. Some chemicals or medications produce an allergic reaction only when exposed to light (usually ultraviolet type A, UVA). Patients who are over-sensitive to light and those with a rash that appears on parts of the body normally exposed to light but that does not appear in areas shielded from the light should have a photo-patch test.

5. Photo Tests is skin irradiation with a specific range of ultraviolet light. Photo tests are performed for the evaluation of photosensitivity disorders.

6. Skin Endpoint Titration (SET) Testing or Intradermal Dilutional Testing (IDT) analyzes the highest dilution of a substance that produces a reaction, and may be used to determine the starting dose(s) of allergen immunotherapy.

7. Delayed Hypersensitivity Skin Testing has been commonly used in three ways: anergy testing, testing for infection with intracellular pathogens, and testing for sensitivity to contact allergens. Accurate testing for contact allergy requires careful attention to technique, and limitation of testing to the specific allergens known to be associated with a contact reaction.

8. Ophthalmic Mucous Membrane Tests and Direct Nasal Mucous Membrane Tests are rarely indicated. They are allowed when skin testing cannot test allergens.

Ophthalmic mucous membrane tests and direct nasal mucous membrane tests are approved if levels of allergic

mediators (such as histamine and tryptase) are measured and a placebo control is performed. This is usually performed in allergy research laboratories. It is also approved in the office setting if the physician is there to observe objective measurement of reactions which might include redness of the eyes, tearing and sneezing.

9. Inhalation Bronchial Challenge Testing involves the inhalation of agents that can trigger respiratory responses and are often used to evaluate new allergens and/or substantiate the role of allergens in patients with significant symptoms. Results of these tests are ordinarily evaluated by objective measures of pulmonary function and occasionally by characterization of bronchoalveolar lavage samples.

a. Inhalation bronchial challenge tests should be performed as dose-response assays where in provocation concentration thresholds can be determined on the basis of allergen concentration required to cause a significant decrease in measured pulmonary function.
b. Inhalation bronchial challenge tests with occupational allergens need to be carefully controlled with respect to dose and duration of exposure. When industrial small molecular weight agents are assessed, tests should be performed under conditions of continuous monitoring of the specific chemical being assessed so as not to exceed the threshold limit level permitted in the workplace.

10. Ingestion (Oral) Challenge Test involves the administration of sequentially or incrementally larger doses of the test item. The test items may include food or antibiotics. The service is allowed once per patient encounter, regardless of the number of items tested, and includes evaluation of the patient's response to the test items.

Challenge ingestion food testing is covered for the following indications:

- Food allergy, dermatitis
- Anaphylactic shock due to adverse food reaction
- Allergy to medicinal agents
- Allergy to foods

Challenge Ingestion is not payable when used to diagnosis rheumatoid arthritis, depression, or respiratory disorders. (CMS Pub. 100-03 *Medicare National Coverage Determination (NCD)Manual,* Chapter 1- Coverage Determinations, Part 2 Section 110.12- Challenge Ingestion Food Testing).

11. Intracutaneous testing, delayed reaction - more than 6 tests, may be covered but requires additional justification and case-by-case review for the number of tests performed and the medical necessity except when the skin test is used:

For collagen implant therapy. Refer to: CMS Pub 100-03 *Medicare National Coverage Determinations (NCD) Manual, Chapter 1* – Coverage Determinations, Part 4, Section 230.10 – Incontinence Control Devices.

12. Organ challenge test materials may be applied to the mucosae of the conjunctivae, nares, GI tract, or bronchi. Considerable experience with these methods is required for proper interpretation and analysis. All organ challenge tests should be preceded by a control test with diluent and, if possible, the procedure should be performed on a double blind or at least single-blind basis.

B. In vitro testing (blood serum analysis): immediate hypersensitivity testing by measurement of allergen-specific serum IgE in the blood serum. They are useful when testing for inhalant allergens (pollens, molds, dust mites, animal danders), foods, insect stings, and other allergens such as drugs or latex, when direct skin testing is

impossible due to extensive dermatitis, marked dermatographism, or in children younger than four years of age.

In vitro testing is covered when skin testing is not possible or would be unreliable; or in vitro testing is medically reasonable and necessary as determined by the physician. When in vitro testing is ordered or performed, the medical record must clearly document the indication and why it is being used instead of skin testing.

It is not covered when done in addition to a skin test for the same antigen, except in the case of suspected latex sensitivity, hymenoptera, or nut/peanut sensitivity where both the skin test and the in-vitro test may be performed. The number of tests done, choice of antigens, frequency of repetition and other coverages issues are the same as skin testing.

Testing must be based on a careful history/physical examination which suggests IgE medicated disease. Total Serum IgE is not appropriate in most general allergy testing. Instead, individual IgE tests are performed against a specific antigen.

Special clinical situations in which specific IgE immunoassays are performed against a specific antigen may be appropriate in the following situations:

1. Patients with extensive dermatitis, severe dermatographism, ichthyosis or generalized eczema that will not make direct skin testing possible.
2. Patients needing continued use of H-1 blockers (antihistamines), or in the rare patient with persistent unexplained negative histamine control.
3. Patients who cannot be safely withdrawn from medications that interfere with skin testing, such as long-acting antihistamines, tricyclic antidepressants, beta-blockers, or medications that may put the patient at undue risk if they are discontinued long enough to perform skin tests.
4. Uncooperative patients with mental or physical impairments.
5. For evaluation of cross-reactivity between insect venoms (e.g., fire ant, bee, wasp, yellow jacket, hornet).
6. As adjunctive laboratory testing for disease activity of allergic bronchopulmonary aspergillosis and certain parasitic disease.
7. To diagnose atopy in small children.
8. Patients at increased risk for anaphylactic response from skin testing based on clinical history (e.g., when an unusual allergen is not available as a licensed skin test extract), or who have a history of a previous systemic reaction to skin testing.
9. Patients in who skin testing were equivocal/inconclusive and in vitro testing is required as a confirmatory test.

Total IgE is reasonable and necessary for follow-up of Allergic Bronchopulmonary Aspergillosis (ABPA) and to diagnosis atopy in children.

Retesting with the same antigen(s) should rarely be necessary within a three-year period. Exceptions include young children with negative skin tests, or older children and adults with negative skin tests in the face of persistent symptoms. Routine repetition of skin tests is not indicated (i.e., annually) and not covered.

Limitations:
The following tests are considered not medically reasonable and necessary:

1. Ingestion (Oral) Challenge Food Testing performed by the patient in the home, and not in the office setting, will not be covered.

2. Provocative Testing for which there is limited or no evidence of validity include the cytotoxic test, the provocation-neutralization procedure, electrodermal diagnosis, applied kinesiology, the "reaginic" pulse test, and chemical analysis of body tissues. Controlled studies for the cytotoxic and provocation-neutralization tests demonstrated that the results are not reproducible and do not correlate with clinical evidence of allergy. Electrodermal diagnosis and applied kinesiology have not been evaluated for efficacy. Similarly, the "reaginic" pulse test and chemical analysis of body tissues for various exogenous chemicals have not been substantiated as valid tests for allergy.

Provocative and neutralization testing and neutralization therapy (Rinkel test) of food allergies (sublingual, intracutaneous and subcutaneous) are excluded from Medicare coverage because available evidence does not show these tests and therapies are effective.

3. IgG and IgG Subclass Antibody Tests measure allergen-specific IgG and IgG subclasses by using immunoabsorption assays and IgG and IgG subclass antibody tests for food allergy/delayed food allergic symptoms or intolerance to specific foods. These tests are considered experimental and investigational since there is insufficient evidence in the published peer-reviewed scientific literature to support the diagnostic value of these tests.

4. Antigens for which no clinical efficacy is documented in peer reviewed literature include the following: newsprint, tobacco smoke and leaf, dandelion, orris root, phenol, alcohol, sugar, yeast, grain mill dust, soybean dust (except when the patient has a known exposure to soybean dust such as a food processing plant), honeysuckle, marigold, goldenrod, fiberglass, wool, green tea, or chalk.

5. Radioallergosorbent test (RAST), fluoroallergosorbent test (FAST), and multiple antigen simultaneous test (MAST) are in vitro techniques for determining whether a patient's serum contains IgE antibodies against specific allergens of clinical importance. As with any allergy testing, the need for such tests is based on the findings during a complete history and physical examination of the patient. These tests are not appropriate in most general allergy testing. Instead, individual IgE tests should be performed against a specific antigen.

6. ELISA (enzyme-linked immunoaorbent assay) test is another in vitro method of allergy testing for specific IgE antibodies against allergens. It is used to determine in vitro reaction to various foods and relies on lymphocyte blastogenesis in response to certain food antigens.

7. Quantitative multi-allergen screen is a non-specific screen that does not identify a specific antigen. It is does not have sufficient literature demonstrating clear cut clinical implication. It is a screening tool and therefore not covered by Medicare.

8. Cytotoxic leukocyte tests are excluded. (CMS Pub. 100-03 *Medicare National Coverage Determination (NCD) Manual,* Chapter 1- Coverage Determinations, Part 2 Section 110.13-Cytotoxic Food Tests).

9. Sublingual intracutaneous and subcutaneous provocative and neutralization testing and neutralization therapy for food allergies are excluded. (CMS Pub 100-03 *Medicare National Coverage Determinations Manual,* Chapter 1- Coverage Determinations, Part 2, Section 110.11 – Food Allergy Testing and Treatment).

10. The following tests are considered **experimental and investigational for allergy testing** as these have not been proven to be effective or appropriate for the evaluation and/or management of IgE-mediated allergic

reactions. This list is not all inclusive:

a. Antigen leukocyte cellular antibody (ALCAT) automated food allergy testing
b. Applied kinesiology or Nambudripad's allergy elimination test (NAET (i.e., muscle strength testing or measurement after allergen ingestion)
c. Anti-Fc epsilon receptor antibodies testing
d. Anti-IgE receptor antibody testing
e. Blood, urine, or stool micro-nutrient assessments
f. Candidiasis test
g. Chemical analysis of body tissues (e.g., hair)
h. Chlorinated pesticides (serum)
i. Chronic urticarial index testing
j. Clifford materials reactivity testing
k. Complement (total or components)
l. Complement antigen testing
m. C-reactive protein
n. Cytokine and cytokine receptor assay
o. Cytotoxic testing for environmental or clinical ecological allergy testing (Bryans Test, ACT)
p. Electrodermal testing or electro-acupuncture
q. Electromagnetic sensitivity syndrome/disorder (allergy to electricity, electro-sensitivity, electrohypersensitivity, and hypersensitivity to electricity).
r. Environmental cultures and chemicals
s. Eosinophil cationic protein (ECP) test
t. Food immune complex assay (FICA) or food allergenic extract immunotherapy
u. General immune system assessments
v. Immune complex assay
w. Immunoglobulin G (IgG) testing for allergy
x. Iridology
y. Leukocyte antibodies testing
z. Leukocyte histamine release test (LHRT)/basophil histamine release test
aa. Lymphocytes (B or T subsets)
ab. Lymphocyte function assay
ac. Mediator release test (MRT) or the LEAP program
ad. Metabolic assessments
ae. Multiple chemical sensitivity syndrome (a.k.a., idiopathic environmental intolerance (IEI), clinical ecological illness, clinical ecology, environmental illness, chemical AIDS, environmental/chemical hypersensitivity disease, total allergy syndrome, cerebral allergy, 20th century disease)
af. Prausnitz-Kustner or P-K testing - passive cutaneous transfer test
ag. Pulse response test
ah. Qualification of nutritional assessments
ai. Rebuck skin window test
aj. Secretory IgA (salvia)
ak. Sage Complement Antigen Test
al. Specific Immunoglobulin (IgG) (e.g., by Radioallergosorbent (RAST) or Enzyme-linked immunosorbent assay (ELISA)
am.Sublingual provocative neutralization testing and treatment with hormones.
an.Total serum IgG, immunoglobulin A (IgA) and immunoglobulin M (IgM
ao. Venom blocking antibodies
ap. Volatile chemical panels (blood testing for chemicals)
aq. Live Cell Analysis
ar. Passive Transfer

as. Cytotoxic Food Testing

Routine allergy re-testing does not meet the definition of medically necessity according to the practice parameters and recommendations from the American College of Allergy, Asthma, and Immunology (ACAAI), the American Academy of Allergy, Asthma, and Immunology (AAAAI), and the Joint Council of Allergy, Asthma, and Immunology (JCAAI).

Summary of Evidence

N/A

Analysis of Evidence
(Rationale for Determination)

N/A

General Information

Associated Information

Documentation Requirements
Adequate documentation is essential for high-quality patient care and to demonstrate the reasonableness and medical necessity of the testing. Documentation must support the criteria for coverage as described in the Coverage Indications, Limitations, and/or Medical Necessity section of this LCD. There should be a permanent record of the allergy test and its interpretation including the test methodology and either the measurement (in mm) of reaction size of both the wheal and erythema response or a standardized grading system for in vivo testing. If in vitro testing is used, instead of skin testing, the medical necessity must be documented. For the in vitro testing, the quantitative result(s) (in kIU/L) for specific IgE must be documented. All patient reaction(s) or complications should be recorded. The report should address or answer any specific clinical questions. If there are factors that prevent answering the clinical questions, this should be explained in the documentation. An official interpretation (final report) of the testing should be included in the patient's medical record. Retention of the allergy test(s) should be consistent both with clinical need and with relevant legal and local health care facility requirements.

The medical record must document the elements of the medical and immunologic history including but not limited to correlation of symptoms; occurrence of symptoms; exposure profile; documentation of allergic sensitization by accepted means and where attempts at avoidance have proven unsuccessful (or the impracticality of avoidance exists); and a copy of the sensitivity results; along with the physical examination. The history should support that attempts to narrow the area of investigation were taken so that the minimal number of necessary skin tests might deliver a diagnosis. Testing results need to justify the diagnosis and code on each claim form. The clinical condition that is claimed to justify this test must be clearly documented in the record. Note: A payable diagnosis alone does not support medical necessity of ANY service. The interpretation of the test results and how the results of the test will be used in the patient's plan of care for treatment and the management of the patient's medical condition (s) must be documented.

Claims submitted without such evidence will be denied as not medically necessary. When the documentation does not meet the criteria for the service rendered or the documentation does not establish the medical necessity for the services, such services will be denied as not reasonable and necessary under Section 1862(a)(1) of the Social Security Act.

All documentation must be maintained in the patient's medical record and made available to Medicare upon request.

Utilization Guidelines

It is expected that these services would be performed as indicated by current medical literature and/or standards of practice. When services are performed in excess of established parameters, they may be subject to review for medical necessity.

It would not be expected that all patients would receive the same tests or the same number of sensitivity tests. The number of tests performed must be judicious and related to the history, physical findings and clinical judgment specific to each individual patient. The selection of antigens should be individualized, based on the history and physical examination.

Retesting with the same antigen(s) should rarely be necessary within a three-year period. Exceptions include young children with negative skin tests or older children and adults with negative skin tests, but persistent symptoms suggestive of allergic disease where skin tests may be repeated one year later. Claims for retesting within a three-year period should be submitted with documentation of the medical necessity.

Testing done on separate days for different antigens is acceptable as long as the total number of tests done within any three-year period is not excessive.

In vitro testing is covered when medically reasonable and necessary as a substitute for skin testing; it is not usually necessary in addition to skin testing. If in vitro testing is inconclusive, and contraindications for skin testing have been resolved, then skin testing may be done and is covered. The medical record must document this rationale. In vitro IgE testing will be limited to 30 allergens/beneficiary over a 12-month period. If more tests are performed, medical records may be requested.

Sources of Information

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Bibliography

N/A

Revision History Information

REVISION HISTORY DATE	REVISION HISTORY NUMBER	REVISION HISTORY EXPLANATION	REASON(S) FOR CHANGE
10/31/2019	R11	10/31/2019 Change Request 10901 Local Coverage Determinations (LCDs): it will no longer be appropriate to include Current Procedure Terminology (CPT)/Health Care Procedure Coding System (HCPCS) codes or International Classification of Diseases Tenth Revision-Clinical Modification (ICD-10-CM) codes in the LCDs. All CPT/HCPCS, ICD-10 codes, and Billing and Coding Guidelines have been removed from this LCD and placed in Billing and Coding: Allergy Testing article linked to this LCD. Consistent with Change Request 10901 language from IOMs and/or regulations has been removed and the applicable manual/regulation has been referenced. Language under Patch Testing and Utilization Guidelines was removed that discussed specific number of tests.	• Other (Compliance with CR 10901)
01/01/2019	R10	01/01/2019 Annual review done 12/05/2018. Typographical error corrected.	• Other (Annual Review)
10/01/2018	R9	10/01/2018 ICD-10 Code updates: added codes T43.641A, T43.641D, T43.641S, T43.642A, T43.642D, T43.642S, T43.643A, T43.643D, T43.643S, T43.644A, T43.644D, and T43.644S to Groups 1 and 2.	• Revisions Due To ICD-10-CM Code Changes
04/01/2018	R8	04/01/2018 - For clarification, added the following bullet point "d. Vaccines" to A. In Vivo Testing under 2. Intracutaneous/Intradermal Tests. Usable codes for vaccines are already listed in Group 1 for intracutaneous/intradermal allergy	• Other

REVISION HISTORY DATE	REVISION HISTORY NUMBER	REVISION HISTORY EXPLANATION	REASON(S) FOR CHANGE
		testing.	
01/01/2018	R7	01/01/2018 CPT/HCPCS code updates: description change to Group 1 code 86003, description change to Group 2 code 86005, and added code 86008 to Group 1 table of codes and to Group 2 Paragraph. Annual review done 12/06/2017	• Revisions Due To CPT/HCPCS Code Changes • Other (Annual Review)
10/01/2017	R6	10/01/2017 ICD-10 code updates: Added the following code to Groups 1, 2 and 3: R06.03. At this time 21st Century Cures Act will apply to new and revised LCDs that restrict coverage which requires comment and notice. This revision is not a restriction to the coverage determination; and, therefore not all the fields included on the LCD are applicable as noted in this policy.	• Revisions Due To ICD-10-CM Code Changes
05/01/2017	R5	05/01/2017 Added diagnosis code K20.0 to Groups 1 and 3. Added verbiage "eosinophilic esophagitis" to indications for percutaneous testing A.1.b.	• Reconsideration Request
02/01/2017	R4	02/01/2017 Annual review done 01/03/2017. Added diagnosis codes T84.89XS and Z91.09 to Group 4 for Patch Tests 95044, 95052. Added a paragraph to clarify patch testing for joint replacement patients. Updated Sources of Information.	• Other (Annual Review)
10/01/2016	R3	10/01/2016 Per ICD-10 code updates: In Group 3: deleted code K52.2 and added codes K52.21, K52.22, K52.29, K52.3, K52.831, K52.832, and K52.838, effective 10/01/2016.	• Revisions Due To ICD-10-CM Code Changes
03/18/2016	R2	08/01/2016 Added codes Z88.0-Z88.8 to Group 5, effective 03/18/2016.	• Revisions Due To ICD-10-CM Code Changes
03/18/2016	R1	04/01/2016 Added initial annual review date into system.	• Other

Associated Documents

Attachments

N/A

Related Local Coverage Documents

Article(s)

A57473 - Billing and Coding: Allergy Testing
A54842 - Response to Comments: Allergy Testing (L36402)
LCD(s)
DL36402
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Related National Coverage Documents

NCD(s)
110.12 - Challenge Ingestion Food Testing
110.13 - Cytotoxic Food Tests
110.11 - Food Allergy Testing and Treatment

Public Version(s)

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MolDX: Biomarkers in Cardiovascular Risk Assessment (L36523)

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Contractor Information

CONTRACTOR NAME	CONTRACT TYPE	CONTRACT NUMBER	JURISDICTION	STATE(S)
Wisconsin Physicians Service Insurance Corporation	MAC - Part A	05101 - MAC A	J - 05	Iowa
Wisconsin Physicians Service Insurance Corporation	MAC - Part B	05102 - MAC B	J - 05	Iowa
Wisconsin Physicians Service Insurance Corporation	MAC - Part A	05201 - MAC A	J - 05	Kansas
Wisconsin Physicians Service Insurance Corporation	MAC - Part B	05202 - MAC B	J - 05	Kansas
Wisconsin Physicians Service Insurance Corporation	MAC - Part A	05301 - MAC A	J - 05	Missouri - Entire State
Wisconsin Physicians Service Insurance Corporation	MAC - Part B	05302 - MAC B	J - 05	Missouri - Entire State
Wisconsin Physicians Service Insurance Corporation	MAC - Part A	05401 - MAC A	J - 05	Nebraska
Wisconsin Physicians Service Insurance Corporation	MAC - Part B	05402 - MAC B	J - 05	Nebraska
Wisconsin Physicians Service Insurance Corporation	MAC - Part A	05901 - MAC A	J - 05	Alabama Alaska Arizona Arkansas California - Entire State Colorado Connecticut Delaware Florida Georgia Hawaii Idaho Illinois Indiana Iowa Kansas Kentucky

CONTRACTOR NAME	CONTRACT TYPE	CONTRACT NUMBER	JURISDICTION	STATE(S)
				Louisiana Maine Maryland Massachusetts Michigan Mississippi Missouri - Entire State Montana Nebraska Nevada New Hampshire New Jersey New Mexico North Carolina North Dakota Ohio Oklahoma Oregon Pennsylvania Rhode Island South Carolina South Dakota Tennessee Texas Utah Vermont Virginia Washington West Virginia Wisconsin Wyoming
Wisconsin Physicians Service Insurance Corporation	MAC - Part A	08101 - MAC A	J - 08	Indiana
Wisconsin Physicians Service Insurance Corporation	MAC - Part B	08102 - MAC B	J - 08	Indiana
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CMS National Coverage Policy

Title XVIII of the Social Security Act (SSA), §1862(a)(1)(A), states that no Medicare payment shall be made for items or services that "are not reasonable and necessary for the diagnosis or treatment of illness or injury or to improve the functioning of a malformed body member."

42 Code of Federal Regulations (CFR) §410.32 Diagnostic x-ray tests, diagnostic laboratory tests, and other diagnostic tests: Conditions.

CMS Pub. 100-02, *Medicare Benefit Policy Manual*, Chapter 15, Section 80-Requirements for Diagnostic X-Ray, Diagnostic Laboratory, and Other Diagnostic Tests

CMS Pub. 100-04, *Medicare Claims Processing Manual*, Chapter 18, Section 100-Preventive and Screening Services, Cardiovascular Disease Screening

CMS Pub. 100-03, *Medicare National Coverage Determinations (NCD) Manual*, Chapter 1, Section 190.23-Lipid Testing.

Coverage Guidance

Coverage Indications, Limitations, and/or Medical Necessity

Under preventative services, Medicare Part B covers the basic lipid panel (total cholesterol, high density lipoprotein-cholesterol (HDL-C), triglycerides, and low-density lipoprotein-cholesterol (LDL-C) for cardiovascular (CV) disease screening, every 5 years when ordered by a doctor.

NCD 190.23 covers lipid panel testing for symptomatic patients for evaluating atherosclerotic CV disease, to monitor the progress of patients on anti-lipid dietary management and pharmacologic therapy for various lipid disorders.

This policy denies coverage for **all CV risk assessment panels,** except the basic lipid panel, for symptomatic (with signs and symptoms) patients with suspected or documented CV disease because panel testing is not specific to a given patient's lipid abnormality or disease. The policy indicates the medical indication(s) based on published scientific articles and consensus guidelines for individual lipid biomarkers that may be covered to characterize a given lipid abnormality or disease, to determine a treatment plan or to assist with intensification of therapy. Each individual lipid biomarkers must be specifically ordered and the reason for the test order documented in the patient's medical record. The policy denies coverage for all **non-lipid** biomarkers when used for CV risk assessment including but not limited to, biochemical, immunologic, hematologic, and genetic biomarkers for CV risk assessment regardless of whether ordered in a panel or individually.

The following biomarkers, when they are included in a CV risk assessment panel, are non-covered:

- Lipoprotein subclasses;
- LDL particles;
- Intermediate density lipoproteins;
- High density lipoprotein AI9LpAI and AI/AII;
- Lipoprotein(a);
- Apolipoprotein B (Apo B), apo A-I and apo E;
- Lipoprotein-associated phospholipase A2 (Lp-PLA2)

- BNP
- Cystatin C
- Thrombogenic/hematologic actors
- Interleukin-6 (IL-6), tissue necrosis factor- a (TNF- a) , plasminogen activator inhibitor-1 (PAI-1) and IL-6 promoter polymorphism
- Free fatty acids
- Visfatin, angiotensin-converting enzyme 1 (ACE2) and serum amyloid A
- Microalbumin
- Myeloperoxidase (MPO)
- Homocysteine and methylenetetrahydrofolate reductase (MTHFR) mutation testing
- Uric acid
- Vitamin D
- White blood cell count
- Long-chain omega-3 fatty acids in red blood cell membranes
- Gamma-glutamyltransferase (GGT)
- Genomic profiling including CardiaRisk angiotensin gene
- Leptin, ghrelin, adiponectin and adipokines including retinol binding protein 4 (RBP4) and resistin
- Inflammatory markers including VCAM-1, P-selectin (PSEL) and E-selectin (ESEL)
- Cardiovascular risk panels

Note #1: There is no Medicare benefit for screening CV risk assessment testing for asymptomatic (without signs or symptoms of disease) patients. Screening asymptomatic patients for cardiovascular risk is statutorily excluded by Medicare and will not be addressed in this policy.

Note #2: FDA approval/clearance means that a test/assay has analytical and clinical validity. The FDA does not review clinical utility (that the test/assay demonstrates improved patient outcomes). To meet Medicare's "reasonable and necessary" criteria for coverage, a test/assay must have proven clinical utility.

Traditional vs Non-traditional CV Risk Assessment
During the last two decades the interest in CV biomarkers as early screening tools has risen dramatically, largely fueled by the recognition that traditional CV risk factors (diabetes, smoking, hypertension and hyperlipidemia) do not fully explain individual variation in CV risk, and by advances in genetic and molecular research. Risk assessment for determining the 10-year risk for developing CHD is traditionally carried out using the Framingham risk score.

Despite the Framingham risk-scoring tool, clinicians have sought non-traditional lipid and other biomarker measurements to predict CV events. The most promising biomarkers are the ones that closely correlate with the pathophysiological process of the disease. In general, there is evidence that some of these biomarkers may alter risk categorization (higher or lower) compared to traditional risk prediction, but it has not been established that changes in categorization provides clinically actionable information beyond that of traditional lipid measures. In addition, no study has provided high-quality evidence that measurement of non-traditional lipid and other biomarkers leads to changes in management that improve health outcomes.

To provide clinically useful knowledge, a biomarker should meet the following criteria:

- Adds clinical knowledge that improves patient outcomes (criteria for Medicare "reasonable and necessary");
- Provides risk information that is independent of established predictors;
- Is easy to measure and interpret in the clinical setting; and
- Is accurate, reproducible and standardized.

High-sensitivity C-reactive protein (hs-CRP)
CRP is a protein produced in the liver during episodes of acute inflammation or infection. The hs-CRP test measures

CRP that is in the normal range for healthy people and is used to distinguish people with low normal levels from those with high normal levels. In recent years, prospective epidemiologic studies have demonstrated that inflammation is essential for CV disease pathogenesis and that high normal levels of hs-CRP correlate with an increased risk of CV events such as myocardial infarction (MI), stroke, sudden cardiac death and peripheral vascular disease (PVD) even when lipid levels are within acceptable ranges. The American Heart Association (AHA) and the US Centers for Disease Control and Prevent (CDC) recommend averaging two hs-CRP levels obtained two weeks apart. Based on hs-CRP test results, they recognize: low (3.0 mg/L) risk groups.

In 2009, the US Preventive Services Task Force (USPSTF) report on the use of non-traditional risk factors noted there is insufficient evidence to recommend the use of non-traditional risk factors to screen asymptomatic individuals with no history of CHD to prevent CHD events. The non-traditional risk factors in their recommendation included: hs-CRP, ankle-brachial index (ABI), leukocyte count, fasting blood glucose level, periodontal disease, carotid intima-media thickness, coronary artery calcification (CAC) score on electron beam computerized tomography (EBCT), homocysteine level, and lipoprotein(a) level. The USPSTF stated there is insufficient evidence to determine the percentage of intermediate-risk individuals who would be reclassified by screening with non-traditional risk factors, other than hs-CRP or ABI. For individuals re-classified as high-risk by hs-CRP or ABI, data are not available to determine whether they benefit from additional treatment. They note the potential harms resulting from re-classification including the use of medications without proven benefit and psychological effects. The USPSTF stated that clinicians should continue to use the Framingham model to assess CHD risk and guide risk-based preventive therapy.

While data from the Physicians' Health Study and Framingham Heart Study have shown that hs-CRP measurements may result in reclassification of an individual's risk compared to standard risk prediction models, meta-analysis including data from the second Northwick Park Heart Study (NPHS II) and the Edinburgh Artery Study concluded that the ability of hs-CRP to reclassify risk correctly was modest and inconsistent.

The Jupiter trial, a randomized, double-blind, placebo-controlled trial of the use of rosuvastatin vs placebo in the primary prevention of CVD in patients without diabetes with LDL-C <130mg/dL and CRP =2 mg/dL, was associated with a significant reduction in the primary endpoint of CV events. These findings suggest that hs-CRP measurement in highly preselected patients may have important clinical implications. However, the Jupiter study was not a trial of hs-CRP because individuals with unknown or low hs-CRP concentrations were not studied. Despite evidence that elevated hs-CRP levels are associated with increased risk of CHD, it has not been determined whether hs-CRP is causally related to CHD.

In 2010, The American College of Cardiology Foundation and the American Heart Association (ACCF/AHA) published guidance as to when and in whom to measure blood levels of hs-CRP. The guidance states that hs-CRP levels may assist in the selection of patients for statin therapy according to the following criteria (Class IIa; Level of evidence (LOE): B):

- Men >50 years of age, or women >60 years of age or older
- LDL-C <130 mg/dL
- Patients not on lipid-lowering, hormone replacement, or immunosuppressant therapy
- Patients without clinical CHD, diabetes, chronic kidney disease, severe inflammatory conditions, or contraindications to statins

For example, a patient may appear to have a low or low-moderate elevated risk of CV events based on traditional risk factor scoring with cholesterol levels, weight, level of exercise, smoking history, diabetes and hypertension. However, an elevated hs-CRP level would indicate that the cardiac risk may be substantially greater than traditional risk factors suggest, and that treatment might be considered. For patients who are already known to have high risk, according to current recommendations, hs-CRP levels will not add any substantially new information, since the patient should already be receiving all available therapy including statins to reduce the risk.

The ACCF/AHA recommended measurement of hs-CRP for CV risk assessment in asymptomatic intermediate-risk men 50 years of age or younger, or women 60 years of age or younger (Class IIb; LOE B). Since screening (asymptomatic patient) is statutorily excluded from coverage, hs-CRP testing for these individuals is not a Medicare benefit. They found no benefit for hs-CRP testing in asymptomatic high-risk adults or men and women below the ages stated above. (Class III; LOE B).

The Canadian Cardiovascular Society guidelines recommend hs-CRP testing in men older than 50 and women older than 60 years of age who are at intermediate risk (10-19%) according to their Framingham risk score and who do not otherwise qualify for lipid-lowering therapy. They also state that subjects who meet Jupiter criteria can be considered for treatment based on the results of that study.

In the National Academy of Clinical Biochemistry's (NACB) practice guidelines on emerging CV risk factors, only hs-CRP met the stated criteria as a biomarker for risk assessment in primary prevention. They recommended:

- If the 10-year predicted risk, after standard global risk assessment, is <5%, hs-CRP should not be measured.
- If the 10-year risk is 5-10%, it is expected that 10% might be reclassified to a higher risk group with the test.
- If the risk is intermediate (10-20%), and uncertainty remains as to the use of preventive therapies such as statins or aspirin, then hs-CRP measurement might be useful for further stratification into a higher or lower risk category.

The NACB also recommended that:

- Therapies based on hs-CRP should be based on a clinician's clinical judgment because benefits of such treatment are uncertain;There is insufficient data that therapeutic monitoring using hs-CRP
- over time is useful to evaluate effects of treatment in primary prevention;
- The utility of hs-CRP levels to motivate patients to improve lifestyle behaviors has not been demonstrated;
- Evidence is inadequate to support concurrent measurement of other inflammatory markers in addition to hs-CRP for coronary risk assessment.

In 2012, the American Association of Clinical Endocrinologist gave a 2b recommendation for the use of hs-CRP to stratify borderline CV risk in patients with a standard risk assessment, or those with an LDL-C<130 mg/dL. A European consensus guideline (2012) recommended that hs-CRP testing should not be measured in asymptomatic low- and high-risk patients and gave a weak recommendation to further stratify patient with an intermediate risk of CVD.

The AHA's statement on non-traditional risk factors and biomarkers in CV disease in youth notes "There is currently no clinical role for measuring CRP routinely in children when assessing or considering therapy for CVD risk factors." The AHA also state that it is not clear whether high hs-CRP levels during childhood and adolescence lead to an increased risk of CVD in adult life. While lifestyle changes have been shown to decrease hs-CRP in children, and statins reduce CRP in adults, the AHA indicates there is minimal information available on the effect of statins on hs-CRP in children and whether lowering hs-CRP in children mitigates preclinical disease or CVD in adulthood. Similarly, the National Heart, Blood and Lung Institute (NHBLI) guideline on CV risk in children and adolescents found insufficient evidence to recommend hs-CRP testing in these patient groups.

In summary, this contractor expects testing to be limited to the following criteria:

1. Patient has intermediate CV risk (10-20% risk of CVD per 10 years using the Framingham point score);**and**
2. Patient has LDL-C between 100-130 mg/dL; **and**

3. Patient has two or more CHD major risk factors, including
    - Age (Men > 50 years; Women > 60 years)
    - Current cigarette smoking
    - Family history of premature CHD (CHD in male first degree relative <55; CHD in female fist degree relative <65 years of age)
    - Hypertension (Systolic > 140 mm Hg, or on anti-hypertensive medication)
    - Low HDL-C (<40 mg/dL)

The use of hs-CRP testing to evaluate the effects of treatment or to motivate patients to improve lifestyle behaviors are not considered medically reasonable and necessary, and therefore not covered by Medicare.

Lipoprotein subclasses

Lipoprotein subclass determination based on density, electric charge and other physical chemistry aspect of particles such as nuclear magnetic resonance allow more specific characterization of the major subclasses (VLDL, LDL, IDL and HDL). Studies showed that small, dense LDL particles were highly associated with the occurrence of CVD and diabetes.

LDL Particles (LDL-P) (aka LDL or Lipoprotein Particles or Particle Number, LDL or Lipid Subfractionation, Lipid Phenotyping, Nuclear Magnetic Resonance or NMR Profile)

Small dense LDL with elevated triglyceride levels and low HDL-cholesterol levels constitute the "atherogenic lipoprotein phenotype" form of dyslipidemia that is a feature of type II diabetes and the metabolic syndrome. Measurement of LDL particle density has been proposed as a technique to further risk stratification in patients with elevated LDL levels or for patients with normal LDL levels who have other high-risk factors for CAD, or to predict response to a particular therapy.

Although great progress has been made in the development of refined lipoprotein assessment and such measurements have helped in understanding the atherosclerotic process, it is not known whether measurements beyond traditional lipids can identify CV risk subgroups and how treatment would differ based on subgroup classification. Furthermore, it is not known whether this additional information helps the health care provider to identify with greater precision and accuracy the person who will develop clinical or subclinical CVD.

The NACB does not recommend testing as there is insufficient data that measurement of lipoprotein subclasses can identify CV risk subgroups, how treatment would differ based on subgroup classification and whether, over time, measurement is useful to evaluate the effects of treatments. In addition, the 2010 ACCF/AHA guidelines for assessment of lipoprotein, other lipoprotein parameters and modified lipids state that "measurement of lipid parameters, including lipoproteins, apolipoproteins, particle size, and density, beyond standard fasting lipid profile is not recommended for cardiovascular disease risk assessment in asymptomatic adults."

Unlike lipoprotein size or subclass measures, which seek to improve CV risk assessment beyond conventional lipid testing, LDL particle number tests (NMR LDL-P) and apoB are simply an alternate measure of LDL quantity. Current data supports the ability of LDL particle number to provide clinically actionable information beyond traditional lipid measures to adjudicate individual response to treatment and guide adjustment in therapy. In addition, recent data demonstrate that patients with established CHD, stroke, TIA, peripheral arterial or diabetes achieving NMR LDL-P < 1000 nmol/L during the course of their normal medical care experienced a significant 22-25% reduction in risk of CV events (myocardial infarction, revascularization, angina and stroke) versus patients managed to LDL-C < 100 mg/dL at 12, 24, and 36 months follow-up.

LDL particle number (NMR LDL-P), rather than LDL size or subclass, has been shown to be significantly associated with CV risk independent of traditional lipid and established risk factors. The American Association of Clinical

Endocrinologists (AACE), the National Lipid Association (NLA), the American Diabetes Association (ADA) in conjunction with the American College of Cardiology (ACC), and the American Association of Clinical Chemistry (AACC) have developed consensus position statement on lipoprotein particle management in individuals at risk for CVD. Due to the prevalence of discordantly elevated LDL-P despite achieving low LDL-C and non-HDL-C values, each endorses use of LDL particle number to evaluate LDL response and aid decision making regarding potential adjustment of therapy. The 2013 AACE Comprehensive Diabetes Management Algorithm, as well as the 2015 joint AACE/American College of Endocrinology Clinical Practice Guidelines for Comprehensive Diabetes Mellitus Care, advocate specific LDL particle number goals for statin treated diabetic patients at high CV risk.

Intermediate Density Lipoproteins (Remnant Proteins)
Intermediate density lipoproteins (IDLs) have a density that falls between LDLs and VLDLs and may be referred to as remnant lipoproteins because they vary in size and contain varying proportion of triglycerides and cholesterol. Although there is abundant evidence the remnant lipoproteins are atherogenic, and a risk factor for CAD, there is no evidence how testing improves patient outcomes.

High Density Lipoprotein (HDL) Subclass (Lipoprotein AI 9LpAI) and Lipoprotein AI/AII (LpAI/AII) and/or HDL3 and HDL2
HDL cholesterol (HDL-C) is the risk indicator most often used in associated with CHD risk. HDL subfractions have been used for risk prediction. However, data is lacking how the subfractions aid in the diagnosis and management of CHD. Neither the NCEP nor ACCF/AHA guidelines recommend the routine measurement of HDL subspecies in CHD risk assessment.

Lipoprotein(a) (Lp(a))
Lp(a) is a modified form of LDL in which a large glycoprotein, apolipoprotein(a) is bound to apolipoprotein B. It promotes foam cell formation and the deposition of cholesterol in atherosclerotic plaques, and, because it is structurally similar to plasminogen, Lp(a) may contribute to clot formation. However, the complete role of lipoprotein(a) is not fully understood.

There is no standardized scale for measuring Lp(a) because there is no level that is considered "normal". Because Lp(a) levels are controlled predominantly by genes, cholesterol-lowering drugs have little effect on lowering Lp(a) levels. Elevated Lp(a) is considered an independent risk factor for cardiovascular events, including myocardial infarction, stroke, CVD, vein graft restenosis, and retinal arterial occlusion and may be used to identify individuals who might benefit from more aggressive treatment of other risk factors. However, regardless of the association between Lp(a) and CV disease, there is no data to suggest that more aggressive risk factor modification improves patient health outcomes.

The NACB specifies that Lp(a) screening is not warranted for primary prevention and assessment of cardiovascular risk. They comment that Lp(a) measurement may be done at the physician's discretion if the risk is intermediate (10%–20%) and uncertainty remains as to the use of preventive therapies such as statins or aspirin (Recommendation – IIb; LOE – C). They further note there is insufficient evidence to support therapeutic monitoring of Lp(a) concentrations for evaluating the effects of treatment.

Similarly, the 2010 ACCF/AHA guidelines conclude that apolipoproteins are not recommended for CV disease risk assessment in asymptomatic adults. UpToDate notes that Lp(a) is a modest, independent risk factor for CVD, especially MI, but notes there are no clinical trials that have adequately tested the hypothesis that Lp(a) reduction reduces the incidence of first or recurrent CVD events.

Lp(a) testing may be indicated in select patients, particularly intermediate risk patient, to assist physicians with the use of preventive therapies. Routine testing is not covered by Medicare.

Apolipoprotein B (Apo B), Apolipoprotein A-I (Apo AI), and Apolipoprotein E (Apo E)
Apo B is a constituent of LDL particles and serves as an indirect measurement of the number of LDL particles.

Consequently, elevated levels of Apo B suggest increased levels of small dense LDL particles that are thought to be atherogenic.

Apo AI is the major protein constituent of HDL-C. However, its measurement has not been established as a clinically useful test in determining clinical therapy for patients with CAD or dyslipemia at the current time.

While Apo B and Apo A-I are thought to be the main structural proteins of atherogenic and anti-artherogenic lipoproteins and particles, testing for these compounds has not been validated as a tool for risk assessment. As such, the 2010 ACCF/AHA guidelines indicate that apolipoproteins testing is not recommended for CV risk assessment in asymptomatic adults. However, AACE recommends Apo B testing to assess residual risk in patients for CAD (even when LDL-C levels are controlled) in patient when the triglyceride concentration is >150 mg/dL or the HDL-C concentration is <40 mg/dL. Medicare expects testing to be limited to assessment of residual risk in patients with CAD with triglyceride concentrations of >150 mg/dL or HDL-C of <40 mg/dL.

Apo E, the major constituent of VLDL and chylomicrons, acts as the primary binding protein for LDL receptors in the liver and is thought to play a role in lipid metabolism. Although some individuals hypothesize that Apo E genotypes may be useful in the selection of drug therapy, the value of Apo E testing in the diagnosis and management of CHD is insufficient and needs further evaluation.

The National Cholesterol Education Program (NCEP) expert panel concluded that Apo AI is carried in HDL and it is usually low when HDL is reduced. A low Apo AI thus is associated with increased risk of CHD, but not independently of low HDL. Whether it has independent predictive power beyond HDL-C is uncertain and its measurement is not recommended for routine risk assessment in Adult Treatment Panel (ATP III) Guidelines.

Testing for Lipoproteins

Apolipoproteins
Apolipoproteins are measured in routine clinical laboratories with the use of immunonephelometric or immunoturbidimetric assays. ApoB reflects the number of potentially atherogenic lipoprotein particles because each particle of VLDL, IDL, LDL and lipoprotein(a) particle carries on its surface 1 Apo B100 protein. Most of plasma Apo B is found in LDL particles. HDL particles do not carry Apo B. Instead they carry Apo AI, which does not correspond directly to the concentration of HDL particles in a 1-to-1 fashion.

LDL Gradient Gel Electrophoresis (GGE) (used by Berkeley Heart Lab, Berkeley, CA)
GGE is the most commonly used lab technique to measure LDL particle density. It has been promoted as an important criteria of CHD risk, and as a guide to drug and diet therapy in patients with CAD. While the measurement of LDL subclass patterns may be useful in elucidating possible atherogenic dyslipemia in patients without abnormal total cholesterol, HDL, LDL and triglycerides, there is inadequate evidence that LDL sub-classification by GGE improves outcomes in patients with CV disease.

Density Gradient Ultracentrifugation (DGU) (used by Atherotec Inc, Birmingham, AL)
The Vertical Auto Profile (VAP) test measures the relative distribution of cholesterol within various lipoprotein subfractions, quantifying the cholesterol content in the VLDL, IDL, LDL, lipoprotein(a) and HDL subclasses. It includes components (e.g., total cholesterol, direct measured LDL-C, HDL-C and triglycerides), LDL density (i.e. pattern A versus pattern B), IDL, HDL sub types, VLDL density and Lp(a), and non-lipid CV risk assessment biomarkers including hs-CRP, homocysteine, Lp-PLA2, Apo-E genotype, vitamin D, cystatin and NT-proBNP.

Nuclear Magnetic Resonance Spectroscopy
In this method (NMR LipoProfile® is FDA cleared and available from LipoScience Inc, Raleigh, NC) particle concentrations of lipoprotein subfractions of different size are obtained from the measured amplitudes of their lipid

methyl group NMR signals. Lipoprotein particle sizes are then derived from the sum of the diameter of each subclass multiplied by its relative mass percentage based on the amplitude of its methyl NMR signal.

Note: FDA clearance does not mean the test has clinical utility.

Ion-Mobility Analysis
This method (available from Quest Diagnostics Inc., Madison, NJ) measures both the size and concentration of lipoprotein particle subclasses on the basis of gas-phase differential electric mobility.

Summary of Lipoprotein Testing
At the current time, none of the above tests for lipoproteins have better predictive strength than total/HDL-C ratio and there has been no clear benefit for measuring particle number in most studies to date. Additional research is needed to establish the utility of following changes in lipoproteins as a therapeutic target and determine if any subgroups of patients benefit.

Lipoprotein-Associated Phospholipase A2 (Lp-PLA2)
Lp-PLA2 is also known as platelet activating factor acetylhydrolase. This enzyme hydrolyzes phospholipids and is primarily associated with LDLs. It has been suggested that this enzyme has a proinflammatory role in the development of atherosclerosis. Studies show that Lp-PLA2 is an independent predictor of CV risk but fail to demonstrate improved health outcomes. To improve outcomes, studies must demonstrate how risk factors improve risk classification and change in physician practice to improve patient outcomes.

The NCEP ATP III panel concluded that routine measurement of inflammatory markers (including Lp-PLA2) for the purpose of modifying LDL-cholesterol goals in primary prevention is not warranted. In the 2010 ACCF/AHA guidelines for assessment of CV risk, the experts concluded "lipoprotein-associated phospholipase (Lp-PLA2) might be reasonable for cardiovascular risk assessment in intermediate risk asymptomatic adults". However, at the current time, it is not known whether Lp-PLA2 concentrations are clinically effective for motivating patients, guiding treatment, or improving outcomes.

B-type Natriuretic Peptide (BNP)
BNP and NT-proBNP, hormones produced by cardiocytes in response to hemodynamic stress, have emerged as preferred biomarkers for assessing heart-related stress. There is evidence that these hormones provide prognostic information of mortality and first CV events beyond traditional risk factors. However, there is currently no evidence that treatment or intervention based on the increased risk implied by these biomarkers improves patient outcomes.

These hormones do play a role in the acute setting for use in diagnosing decompensated heart failure.

Cystatin C
Cystatin C, encoded by the CST3 gene, is a small serine protease inhibitor protein secreted by all functional cells in the body. It is used as a biomarker for renal function, and in CV risk assessment although there is no evidence that this marker improves outcomes when used in clinical care. The NACB guidelines on Biomarkers of Renal Function and Cardiovascular Disease Risk do not recommend testing. The NCEP advocates clinical studies to characterize the utility of these markers in the global assessment of CV disease risk.

Thrombogenic/Hematologic Factors
Hematologic factors including coagulation factors and platelets play a role in acute coronary syndrome although the precise mechanism is not known. That platelets are involved in this process is supported by strong evidence that aspirin and other antiplatelet therapies reduce the risk of myocardial infarction.

Fibrinogen has also been associated with CHD risk. A high fibrinogen level is associated with increased risk for coronary events, independent of cholesterol levels, while a low fibrinogen indicates a reduced risk even with high cholesterol levels. Other hemostatic factors associated with increased coronary risk include, but are not limited to,

activated factor VII (aFVII), tissue plasminogen activator (tPA), plasminogen activator inhibitor-1 (PAI-1), von Willebrand factor (vWF), Factor V Leiden (FVL), Factor II (F2), Protein C (PC) and antithrombin III.

In 2009, the NACB guidelines reported there was sufficient data that fibrinogen is an independent marker of CVD risk. In addition, measurement of fibrinogen was not recommended because they expressed analytical concerns regarding insufficient assay standardization and uncertainty in identifying treatment strategies. Additionally, the NCEP expert panel concluded "ATPIII does not recommend measurement of prothrombotic factors as part of routine assessment of CHD risk". They indicated that the strength of the association between thrombogenic/hemotologic factors and CHD risk has not been defined and recommended clinical trials that target specific prothrombotic factors.

D-dimer is associated with an increased risk of venous and arterial thrombotic events, irrespective of baseline vascular disease, even after adjusting for confounders such as age, smoking and diabetes. In CVD, an increased fibrin turnover represents not only a prothrombotic state, but also is a marker for the severity of atherosclerosis. Although D-dimer is a simple test that is widely available, it remains unclear whether D-dimer plays a causal role in the pathophysiology of CV adverse events, or whether D-dimer is simply a marker of the extent of disease.

Interleukin-6 (IL-6), Tissue Necrosis Factor- a (TNF-a), Plasminogen Activator Inhibitor-1 (PAI-1), and IL-6 Promoter Polymorphism

Adipose tissue is a prominent source of PAI-1. Recent data indicates there is continuous production of large amounts of active PAI-1 in platelets that may contribute to clot stabilization. PAI-1 is the primary physiological inhibitor of plasminogen activation. Increased PAI-1 expression acts as a CV risk factor and plasma levels of PAI-1 strongly correlate with body mass index (BMI). Similar associations have been reported between PAI-1 activity and plasma insulin and triglycercide levels in patients with CAD and diabetes. However, there is no data that PAI-1 testing changes physician management to improve patient outcomes.

IL-6, an inflammatory cytokine, is involved in metabolic regulation of CRP. IL-6 plays an important role in the process of rupture or erosion of atherosclerotic plaques, and its serum levels are elevated during these events. At the current time, there is no consensus on IL-6 assay methods or reference values, and no data that demonstrates IL-6 testing changes physician management to improve patient outcomes.

Early in atherosclerotic plaque formation, leukocytes adhere to and are entrapped in the endothelial wall, a process mediated by inflammatory adhesion molecules such as P-selectin and ICAM-1 that are modulated by TNF-a. However, to date, these biomarkers have not provided additional predictive power above that of traditional lipid markers.

Because a polymorphism in the promoter region of IL-6 (174 bp upstream from the start site) appears to influence the transcription of the IL-6 gene and plasma levels of IL-6, this functional polymorphism was considered a candidate gene in the development of CV disease. However, multiple studies have produced inconsistent findings. In a large population-based study, no significant relationship between IL-6 promoter polymorphism and risk of CHD was identified. The authors concluded that IL-6-174 promoter polymorphism is not a suitable genetic marker for increased risk of CHD in person aged 55 years or older.

Free Fatty Acids (FFA, Saturated and Unsaturated)

The role of plasma FFA in thrombogenesis in humans is poorly established and no strong direct evidence is available. Increasing plasma FFA concentration is known to induce endothelial activation, increase plasma MPO level and promote a prothrombotic state in non-diabetic healthy subjects. Studies are ongoing to demonstrate the role of FFA in the pathogenesis of atherosclerosis. However, at the current time, there is sparse data on its role in early atherosclerosis and no evidence how testing improves patient outcomes.

Visfatin, Angiotensin-Converting Enzyme 2 (ACE2) and Serum Amyloid A

Visfatin is an active player promoting vascular inflammation and associated with atherosclerosis-related disease. It is involved in cytokine and chemokine secretion, macrophage survival, leukocyte recruitment by endothelial cells,

vascular smooth muscle inflammation and plaque destabilization. Although visfatin has emerged as a promising pharmacological target in the context of CV complications, there is no evidence how testing improves patient outcomes.

The renin-angiotensin system (RAS) plays a major role in the pathophysiology of CVD. The enzyme angiotensin-converting enzyme (ACE) converts angiotensin I into the vasoconstrictor, angiotensin II, the main effector of the renin-angiotension system. It has been suggested that circulating ACE2 may be a marker of CVD with low levels of ACE2 in healthy individuals and increased levels in those with CV risk factors or disease. However, larger clinical studies are needed to clarify the role of ACE2 as a biomarker of CVD, determine the prognostic significance of circulating ACE2 activity and assess whether the measurement of ACE2 will improve CVD risk prediction.

Serum amyloid A (SAA) is a sensitive marker of inflammation and its elevation has been implicated in obesity and in CVD. It is a highly conserved acute-phase protein, stimulated by proinflammatory cytokines such as IL-6, TNF, interferon-gamma and transforming growth factor-beta (TGF-B). SAA is also a kind of apolipoprotein that is involved in cholesterol metabolism. However, there is sparse data on its role in early atherosclerosis and no evidence how testing improves patient outcomes.

Microalbumin
Microalbuminuria is both a renal risk factor and a CV risk factor in patients with diabetes, and particularly a risk marker of CV mortality in the general population. Microalbuminuria also appears to be a sensitive marker for detecting new onset of hypertension and diabetes. However, for albuminuria to be a target for therapy, one needs to prove that lowering of albuminuria per se is cardioprotective. Albuminuria-lowering effect of antihypertensive agents, particularly those that interfere with RAS, and the use of statins and glucoseaminoglycans have been proved in randomized, controlled trial to be cardioprotective. However, few have been directed at albuminuria lowering per se to evaluate the effect on CV outcome. The question remains as to whether microalbuminuria is the consequence or the cause of organ damage, particularly whether high levels of albuminuria in young children reflect normal physiological variations in endothelial function associated with CV and renal risk in later age. While albumin excretion levels may represent a primary marker for success of intervention strategies aimed at repairing vascular function, there is no data how testing improves patient outcomes at the current time.

Myeloperoxidase (MPO)
Elevated levels of myeloperoxidase, secreted during acute inflammation, are thought by some to be associated with coronary disease and predictive of acute coronary syndrome in patients with chest pain. Many studies have implicated MPO in the pathogenesis of atherosclerosis, showing that it is enriched within atheromatous plaques. Inflammatory cells recruited into the vascular wall release MPO-derived reactive oxygen species that can promote endothelial dysfunction by reducing the bioavailability of nitric oxide, generate atherogenic oxidized-LDL, and modify HDL, impairing its function in cholesterol efflux. However, at the current time there is insufficient data to demonstrate that plasma MPO can predict CHD independent of other CVD risk factors and there is no data that demonstrates how plasma MPO levels affect management of individuals at risk for or patients with CHD.

PPAR-*y* is a key regulator of fatty acid metabolism, promoting its storage in adipose tissue and reducing circulating levels of free fatty acids. Activation of PPAR-*y* has favorable effects on surrogate measures of adipocyte function, insulin sensitivity, lipoprotein metabolism, and vascular structure and function. However clinical trials of thiazolidinedione PPAR-*y* activators have not provided conclusive evidence that they reduce CV morbidity and mortality.

At the current time, there is no clinical data that demonstrates the clinical utility of testing for lipid peroxidation, isoprostanes, malondialdehyde, nitrotyrosine, S-glutathionylation, oxidized LDL, or oxidized phospholipids. Additionally, genetic testing for genes that regulate cellular and systemic oxidative stress, including but not limited to, nuclear factor-2 (Nrf-2), peroxisome proliferator-activated receptor gamma-co-activator 1alpha (PCG-1a), and the thioredoxin family or proteins have no clinical data that demonstrates utility.

Homocysteine and Methylenetetrahydrofolate Reductase (MTHFR) Mutation Testing
Homocysteine is an amino acid found in the blood. Observational evidence generally supports the association of homocysteine levels with CV risk, particularly observational data that patients with hereditary homocystinuria, an inborn error of metabolism associated with high plasma levels of homocysteine, have markedly increased risk of CV disease. Folic acid and the B vitamins are involved in the metabolism of homocysteine. Several studies found the higher levels of B vitamins are associated with lower homocysteine levels, while other evidence shows that low levels of folic acid are linked to a higher risk of CHD and stroke. However, large randomized controlled trials do not support a protective effect of folic acid supplementation (rectifying homocysteine levels) in cardiovascular disease.

MTHFR is a key enzyme in folate metabolism. Two variants of the MTHFR polymorphisms result in reduced enzyme activity, impaired methylation and increased risk of CVD, stroke, and hypertension. MTHFR mutation testing has been advocated to evaluate the cause of elevated homocysteine levels.

However, in 2009, the US Preventive Services Task Force (USPSTF) concluded that the evidence was insufficient to assess the benefits and harms of using non-traditional risk factors to screen asymptomatic adults with no history of CHD to prevent CHD events. Homocysteine was one of the non-traditional factors considered in the recommendation. In 2010, later updated in March 2014, the AHA stated that a causal link between homocysteine levels and atherosclerosis has not been established and noted that high homocysteine levels is not a major risk factor for CV disease. The 2012 American Association of Clinical Endocrinologists (AACE) guidelines for management of dyslipidemia and prevention of atherosclerosis stated that testing for homocysteine, uric acid, PAI-1 or other inflammatory markers is not recommended.

Uric acid
A recent systemic review and meta-analysis suggests that elevated uric acid levels may modestly increase the risk of stroke and mortality. However, future studies are needed to determine whether lowering uric acid levels has any beneficial effects on stroke risk. Data is inadequate to show that uric acid testing changes physician management to improve patient outcomes.

Vitamin D
Low levels of vitamin D are an independent risk factor for CV death in populations without pre-existing CV disease. However, systematic reviews on interventional vitamin D supplementation and CV disease risk reported that vitamin D supplementation had no effect on cardiovascular disease risk, indicating a lack of a causal relationship.

An additional concern regarding vitamin D testing is the considerable variation between results obtained with the various methods (competitive immunoassays, direct detection by high performance liquid chromatography or liquid chromatography combined with tandem mass spectrometry), as well as between laboratories. Immunoassay technologies are less sensitive and specific for vitamin D than liquid chromatography with or without mass spectrometry.

WBC
A large body of data from prospective studies has established an association of leukocyte count with increased risk for CVD events. Leukocytes are thought to play a role in the development and/or progression of atherosclerotic plaques and their rupture due to their proteolytic capacity and oxidative properties. WBC count is correlated with other coronary disease risk factors, including cigarette smoking, BMI, cholesterol level, HDL-C (inversely), triglycerides, diabetes and blood glucose level, physical activity (inversely) and blood pressure. However, the NACB does not recommend WBC testing because clinical utility in reclassifying risk level and identifying treatment strategies is not known.

Long-chain Omega-3 Fatty Acids in Red Blood Cell (RBC) Membranes
It has been proposed that the fatty acid composition of RBCs are an index of long-term intake of eicosapentaenoic (EPA) plus docosahexaenoic (DPA) acids. The omega-3 fatty acids are considered a new modifiable and clinically relevant risk factor for death from CHD. Most studies to date have focused on the association between fish

consumption and risk of CHD. In the Rotterdam Study, analysis of EPA plus DHA and fish intake was assessed in relation of incident heart failure (HF). With nearly 5300 study individuals, the authors concluded that their findings did not support a major role for fish intake in the prevention of HF. Not only is there no association between fish intake and EPA+DHA levels regarding prevention of HF, there is no scientific evidence regarding how measurements of RBC omega-3 fatty acids composition would affect management of individuals at risk for or patients with CHD. A recent article (Marai, 2014) notes that the available data do not support testing for omega-3 polyunsaturated fatty acids (EPA + DHA) among healthy subjects and patients with specific cardiac diseases.

Gamma-glutamyltransferase (GGT)
GGT, a marker of excessive alcohol consumption or liver disturbance, is an enzyme catalyzing the first step in extracellular degradation of the anti-oxidant gluatathione and is thought to play a role in the atherosclerotic process. Coverage for GGT is limited to the indications and limitations specified in CMS NCD 190.32. Whether serum levels of GGT can aid in the detection of individuals at high risk for incident CV events is under investigation. Despite its potential role in stratifying patient risk, there is no evidence testing improves patient outcomes.

Gene Mutations (any methodology) and Genomic Profiling
Proponents of molecular CV profile testing argue that improvement in CVD risk classification leading to management changes that improve outcomes warrants coverage of these tests. However, the Evaluation of Genomic Applications in Practice and Prevention Working Group (EWG) found insufficient evidence to recommend testing for 9p21 genetic variant or 57 other variants in 28 genes to assess risk for CVD in the general population, specifically heart disease and stroke.

The following genes were included in the EWG's assessment: ACE, AGT, AGTR1, APOB, APOC3, APOE, CBS, CETP, CYBA, CYP11B2, F2, F5, GNB3, GPX1, IL1B, LPL, ITGB3, MTHFR, MTR, MTRR, NOS3, PAI-1, PON1, SELE, SOD2, SOD3, TNF, and 9p21. The EWG found that the magnitude of net health benefit from the use of any of these tests alone or in combination is negligible.

CardiaRisk™ (Myriad, Salt Lake UT) markets a genetic test to identify a mutation in the AGT genes. This test supposedly identifies specific hypertensive patients at increased risk of CV disease and identifies patients likely to respond to antihypertensive drug therapy. However, at the present time there is no literature that points to clinical utility for this test.

Leptin, Ghrelin, Adiponectin, and Adipokines including Retinol Binding Protein 4 (RBP4) and Resistin
Leptin, a satiety factor secreted by adipocytes that is instrumental in appetite regulation and metabolism, is elevated in heart disease. In a recent study, leptin levels and proinflammatory high-density lipoprotein (piHDL) when combined into a risk score (PREDICTS) confers 28-fold increased odds of the presence of any current, progressive, or acquired carotid plaque and significantly associated with higher rates of intima-media thickness. However, there is no data that demonstrates how measurement of leptin levels affects management of individuals at risk for or patients with CHD.

Ghrelin is a hormone produced in the stomach and pancreas that plays a role in hunger and weight gain. In a recent study, ghrelin when incorporated in the CV risk model improved the prediction of CVD events in hypertensive patients with reclassification of roughly 21%. However, there is no evidence how testing improves patient outcomes.

Adiponectin is an adipose-specific hormone that has anti-inflammatory properties and is protective against obesity. Particularly in children, measurement of total adiponectin or high-molecular-weight adiponection (HMW adiponectin) as a biomarker for insulin sensitivity and/or as a risk factor for CVD is gaining support. However, the additive value of adiponectin levels remains unclear and how it changes patient outcomes is not known. It is not recommended clinically in children or adults.

RBP4 is gaining recognition as an adipokine that may play an important role in obesity and insulin resistance. The relationship between RBP4 and other traditional and non-traditional risk factors for CVD, such as inflammatory

factors and/or oxidative stress, have not been confirmed in larger populations, and causality has not been established.

Resistin is an adipokine expressed highly in visceral compared with subcutaneous adipose tissue. In the Study of Inherited Risk of Coronary Atherosclerosis (Reilly, 2003), resistin levels were positively correlated with higher coronary calcium scores and correlated with higher levels of soluble TNF-a, receptor-2, Lp(a), and IL-6. The resistin gene (RETN) polymorphism (bp -420 and +299) leads to increased concentrations of the resistin peptide in circulation, which is associated with cardiomyopathy and CAD. One study suggests that in addition to primary risk factors (total cholesterol, LDL, triglycerides and low concentrations of HDL), resistin cytokine may be a risk factor for CVD. However, there is no clinical role for measuring resistin as no data demonstrates how measurement of resistin levels affects management of individuals at risk for or patients with CHD.

Inflammatory Markers – VCAM-1, ICAM-1, P-selectin (PSEL) and E-selectin (ESEL)
Clinical studies have shown that elevated serum concentrations of cell adhesion molecules such as inter-cellular adhesion molecule-1 (ICAM-1), vascular adhesion molecule-1 (VCAM-1), E-selectin (ESEL) and P-selectin (PSEL) may contribute to CVD through their inflammatory effects on the vascular endothelium and be independent risk factors for atherosclerosis and cardiovascular disease (CVD). However, at the current time, testing for these inflammatory markers has not been confirmed in larger populations, causality has not been established and testing has not resulted in improved patient outcomes.

Summary of Evidence

N/A

Analysis of Evidence
(Rationale for Determination)

N/A

General Information

Associated Information

The patient's medical record must contain documentation that fully supports the medical necessity for services included within this LCD. (See "Coverage Indications, Limitations, and/or Medical Necessity") This documentation includes, but is not limited to, relevant medical history, physical examination, and results of pertinent diagnostic tests or procedures.

Documentation supporting the medical necessity should be legible, maintained in the patient's medical record, and must be made available to the MAC upon request.

Sources of Information

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N/A

Revision History Information

REVISION HISTORY DATE	REVISION HISTORY NUMBER	REVISION HISTORY EXPLANATION	REASON(S) FOR CHANGE
11/01/2019	R10	Change Request 10901 Local Coverage Determinations (LCDs): it will no longer be appropriate to include Current Procedure Terminology (CPT)/Health Care Procedure Coding System (HCPCS) codes or International Classification of Diseases Tenth Revision-Clinical Modification (ICD-10-CM) codes in the LCDs. All CPT/HCPCS, ICD-10 codes, and Billing and Coding Guidelines have been removed from this LCD and placed in the Billing and Coding Article related to this LCD. Consistent with Change Request 10901, if any language from IOMs and/or regulations was present in the LCD, it has been removed and the applicable manual/regulation has been referenced. Review completed 10/30/2019.	• Other (CR 10901)
10/01/2019	R9	09/26/2019-ICD-010 Code update: deleted I48.2, added I48.11, I48.19, I48.20 & I48.21. Description change for I70.238 & I70.248.	• Revisions Due To ICD-10-CM Code Changes
03/01/2019	R8	03/01/2019-removed dx code Z13.220- it is on the Medicare NCD Coding Policy Manual and Change Report as a non-covered diagnostic code.	• Other
10/01/2018	R7	10/01/2018 - Added omitted code I63.49 and removed link in #1 of bibliography.	• Revisions Due To ICD-10-CM Code Changes • Typographical Error
10/01/2018	R6	10/01/2018- ICD-010 code update: deleted E78.4 & added new codes E78.41, E78.49, I63.81, I63.89, I67.858. Additional dx codes added: I63.00, I63.011-I63.013, I63.019, I63.02, I63.031-163.033, 163.039,I63.09, I63.10, I63.111-I63.113, I63.119, I63.12, I63.131-I63.133, I63.139, I63.19, I63.20, I63.211-I63.213, I63.219, I63.22, I63.231-I63.233, I63.239, I63.29, I63.30, I63.311-I63.313, I63.319, I63.321-I63.323, I63.329, I63.331-I63.333, I63.339, I63.341-I63.343, I63.349, I63.39, I63.40, I63.411-I63.413, I63.419, I63.421-I63.423, I63.429, I63.431-I63.433, I63.439, I63.441-I63.443, I63.449, I63.49, I63.50, I63.511- I63.513, I63.519, I63.521-I63.523, I63.529, I63.531-I63.533, I63.539, I63.541-I63.543,I63.549, I63.59, I63.9. Annual review completed 09/05/2018. Updated the bibliography section-added numbering and #16 reference and two links.	• Revisions Due To ICD-10-CM Code Changes

REVISION HISTORY DATE	REVISION HISTORY NUMBER	REVISION HISTORY EXPLANATION	REASON(S) FOR CHANGE
04/01/2018	R5	04/01/2018-Annual review completed 03/08/2018. At this time, 21st Century Cures Act will apply to new and revised LCDs that restrict coverage which requires comment and notice. This revision is not a restriction to the coverage determination; and, therefore not all the fields included on the LCD are applicable as noted in this policy.	• Other (Annual Review)
05/01/2017	R4	05/01/2017-Annual Review completed 04/03/2017. Added Note #1: There is no Medicare benefit for screening CV risk assessment testing for asymptomatic (without signs or symptoms of disease) patients. Screening asymptomatic patients for cardiovascular risk is statutorily excluded by Medicare and will not be addressed in this policy. Renumbered previous note 1 to note 2. Updated source of Information section with American Heart Association. AHA Recommendation: Homocysteine, Folic Acid and Cardiovascular Risk &National Academy of Clinical Biochemistry: Laboratory Medicine Practice Guidelines, Emerging biomarkers for primary prevention of cardiovascular disease and stroke. April, 2009. Removed: Due to the level of evidence, there will be no coverage for intermediate risk because there is no data to suggest that more aggressive risk factor modification improves patient health outcomes & Consequently, lipoprotein testing is considered investigational and not covered. Contractor Determination Number: CV-050 is being changed to MolDX-003.	• Other (Annual Review)
01/01/2017	R3	01/01/2017-Code update-83704 code description change.	• Revisions Due To CPT/HCPCS Code Changes • Other (2017 CPT/HCPCs code update)
10/01/2016	R2	10/01/2016- Clarification; The following changes were made in the summary paragraph for High sensitivity C-reactive protein (hs-CRP): Removed first bullet point "1. Men must be > 50 years of age; women must be > 60 years of age; In the first bullet changed the age for Men from >45 to >50 and Women from >55 to >60, changed bullets to numbers for 1-3.Code update- removed deleted code E78.0 and added E78.00 & E78.01.	• Other • Revisions Due To ICD-10-CM Code Changes
06/16/2016	R1	04/27/2016 - Corrected HTML coding for italicized "y" in term PPAR-*y* to allow characters to display correctly. Policy was incorrectly displaying a "?" symbol in error. No other changes to policy.	• Typographical Error

Associated Documents

Attachments

N/A

Related Local Coverage Documents

Article(s)
A55235 - Billing and Coding: MolDX: Arrhythmogenic Right Ventricular Dysplasia/Cardiomyopathy (ARVD/C) Testing
A57559 - Billing and Coding: MolDX: Biomarkers in Cardiovascular Risk Assessment
A55003 - Response to Comments: MolDX: Biomarkers in Cardiovascular Risk Assessment (L36523)
LCD(s)
DL36523
- (MCD Archive Site)

Related National Coverage Documents

NCD(s)
190.23 - Lipid Testing

Public Version(s)

Updated on 11/14/2019 with effective dates 11/01/2019 - N/A
Updated on 09/16/2019 with effective dates 10/01/2019 - 10/31/2019
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Keywords

N/A

Local Coverage Determination (LCD): Drug Testing (L34645)

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Contractor Information

CONTRACTOR NAME	CONTRACT TYPE	CONTRACT NUMBER	JURISDICTION	STATE(S)
Wisconsin Physicians Service Insurance Corporation	MAC - Part A	05101 - MAC A	J - 05	Iowa
Wisconsin Physicians Service Insurance Corporation	MAC - Part B	05102 - MAC B	J - 05	Iowa
Wisconsin Physicians Service Insurance Corporation	MAC - Part A	05201 - MAC A	J - 05	Kansas
Wisconsin Physicians Service Insurance Corporation	MAC - Part B	05202 - MAC B	J - 05	Kansas
Wisconsin Physicians Service Insurance Corporation	MAC - Part A	05301 - MAC A	J - 05	Missouri - Entire State
Wisconsin Physicians Service Insurance Corporation	MAC - Part B	05302 - MAC B	J - 05	Missouri - Entire State
Wisconsin Physicians Service Insurance Corporation	MAC - Part A	05401 - MAC A	J - 05	Nebraska
Wisconsin Physicians Service Insurance Corporation	MAC - Part B	05402 - MAC B	J - 05	Nebraska
Wisconsin Physicians Service Insurance Corporation	MAC - Part A	05901 - MAC A	J - 05	Alabama Alaska Arizona Arkansas California - Entire State Colorado Connecticut Delaware Florida Georgia Hawaii Idaho Illinois Indiana Iowa Kansas Kentucky

CONTRACTOR NAME	CONTRACT TYPE	CONTRACT NUMBER	JURISDICTION	STATE(S)
				Louisiana Maine Maryland Massachusetts Michigan Mississippi Missouri - Entire State Montana Nebraska Nevada New Hampshire New Jersey New Mexico North Carolina North Dakota Ohio Oklahoma Oregon Pennsylvania Rhode Island South Carolina South Dakota Tennessee Texas Utah Vermont Virginia Washington West Virginia Wisconsin Wyoming
Wisconsin Physicians Service Insurance Corporation	MAC - Part A	08101 - MAC A	J - 08	Indiana
Wisconsin Physicians Service Insurance Corporation	MAC - Part B	08102 - MAC B	J - 08	Indiana
Wisconsin Physicians Service Insurance Corporation	MAC - Part A	08201 - MAC A	J - 08	Michigan
Wisconsin Physicians Service Insurance Corporation	MAC - Part B	08202 - MAC B	J - 08	Michigan

LCD Information

Document Information

LCD ID
L34645

LCD Title
Drug Testing

Proposed LCD in Comment Period
N/A

Source Proposed LCD
N/A

AMA CPT / ADA CDT / AHA NUBC Copyright Statement

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Notice Period Start Date
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CMS National Coverage Policy

Italicized font represents CMS national language/wording copied directly from CMS Manuals or CMS transmittals. Contractors are prohibited from changing national language.

Title XVIII of the Social Security Act section 1862 (a) (1) (A). This section excludes coverage and payment of those items or services that are not considered to be medically *reasonable and necessary for the diagnosis or treatment of illness or injury or to improve the functioning of a malformed body member.*

Title XVIII of the Social Security Act section 1862 (a) (1) (D). This section states that no Medicare payment may be made under part A or part B for any expenses incurred for items or services that are investigational or experimental.

Title XVIII of the Social Security Act, Section 1862(a)(7). This section excludes routine physical examinations and services.

Title XVIII of the Social Security Act, Section 1833(e) states that no payment shall be made to any provider for any claim that lacks the necessary information to process the claim.

Code of Federal Regulations (CFR) Title 42, Part 410.32 indicates that diagnostic tests may only be ordered by the treating physician (or other treating practitioner acting within the scope of his or her license and Medicare requirements) who furnishes a consultation or treats a beneficiary for a specific medical problem and who uses the results in the management of the beneficiary's specific medical problem. Tests not ordered by the physician (or other qualified non-physician provider) who is treating the beneficiary are not reasonable and necessary (see section 411.15 (k) (1) of this chapter).
Medicare regulations at 42 CFR 410.32(a) state in part, that "…diagnostic tests must be ordered by the physician who is treating the beneficiary, that is, the physician who furnishes a consultation or treats a beneficiary for a specific medical problem and who uses the results in the management of the beneficiary's specific medical problem." Thus, except where other uses have been authorized by statute, Medicare does not cover diagnostic testing used for routine screening or surveillance.

CMS Pub 100-03 Medicare National Coverage Determination Manual, Chapter 1 – Coverage Determinations, Part 2, Sections 130.5 – Treatment of Alcoholism and Drug Abuse in a Freestanding Clinic and 130.6 – Treatment of Drug Abuse (Chemical Dependency).

CMS IOM Publication 100-08, Medicare Program Integrity Manual, Chapter 13, Section 13.5.4 - Reasonable and Necessary Provisions in an LCD.

Change Request 10901, Local Coverage Determinations (LCDs)

Coverage Guidance

Coverage Indications, Limitations, and/or Medical Necessity

A qualitative/presumptive drug screen is used to detect the presence of a drug in the body. A blood or urine sample may be used. However, urine is the best specimen for broad screening, as blood is relatively insensitive for many common drugs, including psychotropic agents, opioids, and stimulants.
Common methods of drug analysis include chromatography, immunoassay, chemical ("spot") tests, and

spectrometry.

Analysis is comparative, matching the properties or behavior of a substance with that of a valid reference compound (a laboratory must possess a valid reference agent for every substance that it identifies). Drugs or classes of drugs are commonly assayed by qualitative/presumptive testing. A test may be followed by confirmation with a second method, only if there is a positive or negative inconsistent finding from the qualitative/presumptive test in the setting of a symptomatic patient, as described below.

Examples of drugs or classes of drugs that are commonly assayed by qualitative/presumptive tests, followed by confirmation with a second method, are: alcohols, amphetamines, barbiturates/sedatives, benzodiazepines, cocaine and metabolites, methadone, antihistamines, stimulants, opioid analgesics, salicylates, cardiovascular drugs, antipsychotics, cyclic antidepressants, and others. Focused drug screens, most commonly for illicit drug use, may be more useful clinically.

Indications:

A. Although technology has provided the ability to measure many toxins, most toxicological diagnoses and therapeutic decisions are made based on historical or clinical considerations:
    1. Laboratory turnaround time can often be longer than the critical intervention time course of an overdose.
    2. The cost and support of maintaining the instruments, staff training, and specialized labor involved in some analyses are prohibitive.
    3. For many toxins there are no established cutoff levels of .toxicity, making interpretation of the results difficult.

    Although comprehensive screening is unlikely to affect emergency management, the results may assist the admitting physicians in evaluating the patient if the diagnosis remains unclear. Screening panels should be used when the results will alter patient management or disposition.

B. A qualitative/presumptive drug test may be indicated for a variety of reasons including the following:
    1. A symptomatic patient when the history is unreliable, when there has been a suspected multiple-drug ingestion, to determine the cause of delirium or coma, or for the identification of specific drugs that may indicate when antagonists may be used.
    2. For monitoring patient compliance during active treatment for substance abuse or dependence.
    3. To monitor for compliance/adherence to the treatment plan or illicit drug use in patients under treatment or seeking treatment for a chronic pain condition. The clinical utility of drug tests in the emergency setting may be limited because patient management decisions are unaffected, since most therapy for drug poisonings is symptom directed and supportive.
C. Medicare will consider performance of a qualitative/presumptive drug test reasonable and necessary when a patient presents with suspected drug overdose and one or more of the following conditions:
    1. Unexplained coma
    2. Unexplained altered mental status in the absence of a clinically defined toxic syndrome or toxidrome
    3. Severe or unexplained cardiovascular instability (cardiotoxicity)
    4. Unexplained metabolic or respiratory acidosis in the absence of a clinically defined toxic syndrome or toxidrome
    5. Testing on neonates suspected of prenatal drug exposure
    6. Seizures with an undetermined history
D. Medicare will consider performance of a qualitative/presumptive drug test reasonable and necessary when a patient presents with one or more of the following conditions:
    1. For monitoring patient compliance during active treatment for substance abuse or dependence.
    2. A drug screen is considered medically reasonable and necessary in patients on chronic opioid therapy:
    - In whom illicit drug use, non-compliance or a significant pre-test probability of non-adherence to the

prescribed drug regimen is suspected and documented in the medical record; and/or
- In those who are at high risk for medication abuse due to psychiatric issues, who have engaged in aberrant drug-related behaviors, or who have a history of substance abuse.

3. Medicare will consider performance of a drug test reasonable and necessary in patients with chronic pain to:
   - determine the presence of other substances prior to initiating pharmacologic treatment
   - detect the presence of illicit drugs
   - monitor adherence to the plan of care

Drugs, or drug classes for which testing is performed, should reflect only those likely to be present, based on the patient's medical history, current clinical presentation, and illicit drugs that are in common use. Drugs for which specimens are being tested must be indicated by the referring provider in a written order.

A drug test may be reasonable and necessary for patients with known substance abuse or dependence, only when the clinical presentation has changed unexpectedly and one of the above indications is met.

A drug test may be reasonable and necessary for patients with symptoms of schizophrenia suspected to be secondary to drug or substance intoxication.

Definitive drug testing is indicated when:

1. The results of the screen are presumptively positive.
2. Results of the screen are negative and this negative finding is inconsistent with the patient's medical history.
3. This test may also be used, when the coverage criteria of the policy are met AND there is no presumptive test available, locally and/or commercially, as may be the case for certain synthetic or semi-synthetic opioids.

A positive screen often results in an inadequate result upon which to make a proper determination. A more specific method, such as gas or liquid chromatography coupled with mass spectrometry, may be needed in order to obtain a confirmed analytical result. In particular, screens are frequently inadequate for interpretation of opiate and benzodiazepine results and therefore; quantitative testing may be needed in these instances. Confirmation testing is usually not required for drugs like methadone, wherein false positive results are rare. However, factors such as cross-reactivity with other similar compounds or interfering substances in the specimen may affect test results. Confirmatory testing eliminates the risk of false positives. Also, eliminated by confirmation, is the risk of a “pill scraper” slipping through. Patients diverting their drug, attempt to cheat the test by scraping a bit of drug from a pill into their urine sample. It would screen positive, but there would be no metabolite upon confirmation. Frequent use of this code will be monitored for appropriateness.

Limitations:
It is considered not reasonable or necessary to test for the same drug with both a blood and a urine specimen simultaneously.

Drug screening for medico-legal purposes (e.g., court-ordered drug screening) or for employment purposes (e.g., as a pre-requisite for employment or as a requirement for continuation of employment) are not covered.

Summary of Evidence

NA

Analysis of Evidence
(Rationale for Determination)

NA

General Information

Associated Information

Documentation Requirements

1. All documentation must be maintained in the patient's medical record and available to the contractor upon request.
2. Every page of the record must be legible and include appropriate patient identification information (e.g., complete name, dates of service(s)). The record must include the identity of the physician or non-physician practitioner responsible for and providing the care to the patient.
3. The submitted medical record should support the use of the selected diagnosis code(s). The submitted CPT/HCPCS code should describe the service performed.
4. Medical record documentation (e.g., history and physical, progress notes) maintained by the ordering physician/treating physician must indicate the medical necessity for performing a drug test. All tests must be ordered in writing by the treating provider and all drugs/drug classes to be tested must be indicated in the order.
5. If the provider of the service is other than the ordering/referring physician, that provider must maintain hard copy documentation of the lab results, along with copies of the ordering/referring physician's order for the drug test. The physician must include the clinical indication/medical necessity in the order for the drug test.

Sources of Information

Christo, P.J., & et. al. (2011). Urine drug testing in chronic pain. *Pain Physician*, 14: 123-143.

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Jackman, R.P. and Purvis, J.M. (2008). Chronic nonmalignant pain in primary care. *American Family Physician, 78* (10): 1155-1162.

Melanson, S., & et. al. (2010) Interpretation and utility of drug of abuse immunoassays: Lessons from laboratory drug testing surveys. *Archives of Pathology and Laboratory Medicine, 134*: 736-739.

Paulozzi, L., & et al. (2012). CDC grand rounds: prescription drug overdoses-a U.S. epidemic. *JAMA, 307* (8): 774-

776.

Other Contractor(s)' Policies

Bibliography

NA

Revision History Information

REVISION HISTORY DATE	REVISION HISTORY NUMBER	REVISION HISTORY EXPLANATION	REASON(S) FOR CHANGE
11/01/2019	R17	11/01/2019 Added related NCD to Associated Documents. Format revisions completed. No change in coverage.	• Other ((Changes in response to CMS Change Request 10901, Review completed.))
08/29/2019	R16	08/29/2019 Change Request 10901 Local Coverage Determinations (LCDs): it will no longer be appropriate to include Current Procedure Terminology (CPT)/Health Care Procedure Coding System (HCPCS) codes or International Classification of Diseases Tenth Revision-Clinical Modification (ICD-10-CM) codes in the LCDs. All CPT/HCPCS, ICD-10 codes, and Billing and Coding Guidelines have been removed from this LCD and placed in Billing and Coding: Drug Testing linked to this LCD. The applicable manual/regulation has been referenced in CMS National Coverage Policy Section. Review completed 08/08/2019. There will not be a lapse in coverage and there has been no change to the coverage content of this LCD.	• Other (Changes in response to CMS Change Request 10901, Review completed.)
12/01/2018	R15	12/01/2018 Annual review completed on 11/05/2018 with punctuation error corrected. No changes in coverage.	• Other (Annual Review)
10/01/2018	R14	10/01/2018 ICD-10 CM Code Updates: added codes F12.23, F12.93, T43.641A, T43.641D, T43.641S, T43.642A, T43.642D, T43.642S, T43.643A, T43.643D, T43.643S, T43.644A, T43.644D, and T43.644S to Group One.	• Revisions Due To ICD-10-CM Code Changes
01/01/2018	R13	01/01/2018 CPT/HCPCS code updates; description changes for Group 1 codes 80305, 80306, and 80307.	• Revisions Due To CPT/HCPCS Code Changes

REVISION HISTORY DATE	REVISION HISTORY NUMBER	REVISION HISTORY EXPLANATION	REASON(S) FOR CHANGE
12/01/2017	R12	12/01/2017 Annual review completed on 11/07/2017 with no changes in coverage. Typographical error corrected.	• Typographical Error • Other (Annual)
08/01/2017	R11	08/01/2017 Added F11.23 to Group 1 Codes effective 08/01/2017. Corrected typographical errors. At this time 21st Century Cures Act will apply to new and revised LCDs that restrict coverage which requires comment and notice. This revision is not a restriction to the coverage determination; and, therefore not all the fields included on the LCD are applicable as noted in this policy.	• Typographical Error • Other (Added ICD-10-CM Code)
01/01/2017	R10	03/01/2017 Moved G0659 from the Group 1 Paragraph to the Group 1 Table. Long description change for Group 1 codes: G0480, G0481, G0482, and G0483 effective 01/01/2017.	• Revisions Due To CPT/HCPCS Code Changes
01/01/2017	R9	02/01/2017 HCPCS code G0659 added effective 01/01/2017.	• Revisions Due To CPT/HCPCS Code Changes
01/01/2017	R8	01/01/2017 CPT code changes added codes 80305, 80306 and 80307. Deleted codes 80300, 80301, 80302, 80303, 80304, G0477, G0478 and G0479. Annual review 12/02/2016.	• Revisions Due To CPT/HCPCS Code Changes
08/01/2016	R7	08/01/2016- changed CPT descriptions to short description no change in coverage.	• Other
01/01/2016	R6	02/01/2016: Added G0477, G0478, G0479, G0480, G0481, G0482, and G0483 to Group 1 codes section as technically unable to do so last month.	• Other
01/01/2016	R5	01/01/2016 Annual review 12/04/2015. CPT/HCPCS code updates for 2016: G0431, G0434, and G6058 are deleted and added G0477, G0478, G0479, G0480, G0481, G0482, and G0483 to Group 1 codes. Added code range 80320-80377 to Group 2 non-covered codes. Added Z03.89 to Group 1 Paragraph codes. CAC information removed.	• Revisions Due To CPT/HCPCS Code Changes • Other (CPT/HCPCS code changes ICD 10 code additions Other

REVISION HISTORY DATE	REVISION HISTORY NUMBER	REVISION HISTORY EXPLANATION	REASON(S) FOR CHANGE
			) • Revisions Due To ICD-10-CM Code Changes
10/01/2015	R4	10/06/2015 - Due to CMS guidance, we have removed the Jurisdiction 8 Notice and corresponding table from the CMS National Coverage Policy section. No other changes to policy or coverage.	• Other
10/01/2015	R3	04/01/2015 Annual review 03/02/2015, added codes T40.5X1A, T40.5X2A, T40.5X3A, and T40.5X4A. "qualitative" was removed from Indications D 3. Updated sources of information.	• Other (Revisions due to ICD 10 addition Annual Review) • Revisions Due To ICD-10-CM Code Changes
10/01/2015	R2	01/01/2015 CPT/HCPCS code updates 2015, added codes G6058, 80300,80301, 80302, 80303 and 80304 Deleted codes 80100, 80101 and 80102. Removed Qualitative from title and Changed references from qualitative to qualitative/ presumptive to reflect new reporting mechanisms in CPT for 2015.	• Revisions Due To CPT/HCPCS Code Changes
10/01/2015	R1	05/01/2014 Annual review 03/26/2014, no change to policy coverage.	• Other (Maintenance)

Associated Documents

Attachments

N/A

Related Local Coverage Documents

Article(s)
A56915 - Billing and Coding: Drug Testing

Related National Coverage Documents

NCD(s)
130.6 - Treatment of Drug Abuse (Chemical Dependency)
130.5 - Treatment of Alcoholism and Drug Abuse in a Freestanding Clinic

Public Version(s)

Updated on 11/01/2019 with effective dates 11/01/2019 - N/A

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Keywords

- N/A

Local Coverage Determination (LCD): Vitamin D Assay Testing (L34658)

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Contractor Information

CONTRACTOR NAME	CONTRACT TYPE	CONTRACT NUMBER	JURISDICTION	STATE(S)
Wisconsin Physicians Service Insurance Corporation	MAC - Part A	05101 - MAC A	J - 05	Iowa
Wisconsin Physicians Service Insurance Corporation	MAC - Part B	05102 - MAC B	J - 05	Iowa
Wisconsin Physicians Service Insurance Corporation	MAC - Part A	05201 - MAC A	J - 05	Kansas
Wisconsin Physicians Service Insurance Corporation	MAC - Part B	05202 - MAC B	J - 05	Kansas
Wisconsin Physicians Service Insurance Corporation	MAC - Part A	05301 - MAC A	J - 05	Missouri - Entire State
Wisconsin Physicians Service Insurance Corporation	MAC - Part B	05302 - MAC B	J - 05	Missouri - Entire State
Wisconsin Physicians Service Insurance Corporation	MAC - Part A	05401 - MAC A	J - 05	Nebraska
Wisconsin Physicians Service Insurance Corporation	MAC - Part B	05402 - MAC B	J - 05	Nebraska
Wisconsin Physicians Service Insurance Corporation	MAC - Part A	05901 - MAC A	J - 05	Alabama Alaska Arizona Arkansas California - Entire State Colorado Connecticut Delaware Florida Georgia Hawaii Idaho Illinois Indiana Iowa Kansas Kentucky

CONTRACTOR NAME	CONTRACT TYPE	CONTRACT NUMBER	JURISDICTION	STATE(S)
				Louisiana Maine Maryland Massachusetts Michigan Mississippi Missouri - Entire State Montana Nebraska Nevada New Hampshire New Jersey New Mexico North Carolina North Dakota Ohio Oklahoma Oregon Pennsylvania Rhode Island South Carolina South Dakota Tennessee Texas Utah Vermont Virginia Washington West Virginia Wisconsin Wyoming
Wisconsin Physicians Service Insurance Corporation	MAC - Part A	08101 - MAC A	J - 08	Indiana
Wisconsin Physicians Service Insurance Corporation	MAC - Part B	08102 - MAC B	J - 08	Indiana
Wisconsin Physicians Service Insurance Corporation	MAC - Part A	08201 - MAC A	J - 08	Michigan
Wisconsin Physicians Service Insurance Corporation	MAC - Part B	08202 - MAC B	J - 08	Michigan

LCD Information

Document Information

LCD ID
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LCD Title
Vitamin D Assay Testing

Proposed LCD in Comment Period
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Retirement Date
N/A

Notice Period Start Date
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Notice Period End Date
N/A

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CMS National Coverage Policy

Title XVIII of Social Security Act, Section 1861 Act provides for payment of clinical laboratory services under Medicare Part B. Clinical laboratory services involve the biological, microbiological, serological, chemical, immunohematological, hematological, biophysical, cytological, pathological, or other examination of materials derived from the human body for the diagnosis, prevention, or treatment of a disease or assessment of a medical condition.

Title XVIII of Social Security Act, Section 1862(a)(1)(A) excludes expenses incurred for items or services which are not reasonable and necessary for the diagnosis or treatment of illness or injury or to improve the functioning of a malformed body member.

Title XVIII of Social Security Act, Section 1833(e) prohibits Medicare payment for any claim which lacks the necessary information to process the claim.

42 CFR part 493, laboratory services must meet all applicable requirements of the Clinical Laboratory Improvement Amendments of 1988 (CLIA), as set forth. Section 1862(a)(1)(A) provides that Medicare payment may not be made for services that are not reasonable and necessary.

42 CFR 410.32(a), clinical laboratory services must be ordered and used promptly by the physician who is treating the beneficiary.

42 CFR 410.32(a) (3), or by a qualified nonphysician practitioner.

CMS Pub 100-02, *Medicare Benefit Policy Manual*, Chapter 15 - Covered Medical and Other Health Care Services, §80.1 – Clinical Laboratory Services and 80.6 – Requirements for Ordering and Following Orders for Diagnostic Tests.

CMS Pub. 100-04, *Medicare Claims Processing Manual*, Chapter 1- General Billing Requirements, Sections 60 – Provider Billing of Non-covered Charges on Institutional Claims – 60.1.1 - Basic Payment Liability Conditions.

CMS Pub 100-04, *Medicare Claims Processing Manual*, Chapter 25 – Completing and Processing the Form CMS-1450 Data Set, Section 75.5 – From Locators 43-81, FL-67 Principal Diagnosis Codes.

CMS Transmittal No, 857, effective date October 3, 2018 Change Request 10901 Local Coverage Determinations (LCDs) Implementation date January 8, 2019.

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Coverage Guidance

Coverage Indications, Limitations, and/or Medical Necessity

Vitamin D is a hormone, synthesized by the skin, the liver, and then metabolized by the kidney to an active hormone, calcitriol. An excess of vitamin D may lead to hypercalcemia. Vitamin D deficiency may lead to a variety of disorders. This LCD identifies the indications and limitations of Medicare coverage and reimbursement for these services.

Vitamin D is called a "vitamin" because of its availability from an exogenous source, predominately from oily fish in the form of cholecalciferol, vitamin D3. Plant-based vitamin D is in the form of ergocalciferol, Vitamin D2. It is really a hormone, as it is synthesized by the skin, metabolized by the liver and converted by the kidney to an active hormone, calcitriol. Calcitriol in its classical action, absorbs calcium from the intestine, and promotes bone mineralization.

In the skin, 7-dehydrocholesterol is converted to vitamin D3 in response to sunlight, a process that is inhibited by sunscreen with a skin protection factor (SPF) of 8 or greater. Once in the blood, vitamin D2 or D3 from diet, or D3 from skin production are carried by an alpha-2-globulin, vitamin D binding protein, and are carried to the liver where they are hydroxylated to yield 25-hydroxyvitamin D (25OHD; calcidiol). 25OHD then is converted in the kidney to 1, 25(OH)2D (calcitriol) by the action of 25OHD-1-alpha hydroxylase (CYP27B1). The CYP27B1 in the kidney is regulated by nearly every hormone involved in calcium homeostasis, and its activity is stimulated by PTH, estrogen, calcitonin, prolactin, growth hormone, low calcium levels, and low phosphorus levels. Its activity is inhibited by calcitriol, thus providing the feedback loop that helps regulates its synthesis.

An excess of vitamin D is unusual, but may lead to hypercalcemia. Vitamin D deficiency may lead to a variety of disorders; the well-described is rickets in growing children or osteomalacia in adults. Evaluating the status of a patient’s vitamin D sufficiency is accomplished by measuring the level of 25-hydroxyvitamin D. Measurement of other metabolites is generally not necessary outside of several unusual metabolic bone disorders or in chronic kidney disease-mineral bone disorder (CKD-MBD).

Indications:
Measurement of vitamin D levels is indicated for patients with:

- chronic kidney disease stage III or greater;
- osteoporosis;
- osteomalacia;
- osteopenia;
- osteogenesis imperfecta;
- osteosclerosis;
- hypocalcemia;
- hypercalcemia;
- hypoparathyroidism;
- hyperparathyroidism;
- rickets;
- vitamin D deficiency to monitor the efficacy of replacement therapy;
- fibromyalgia;
- granuloma forming diseases;
- hypovitaminosis D;
- hypervitaminosis D;
- long term use of anticonvulsants or glucocorticoids and other medications known to lower - vitamin D levels;
- malabsorption states;
- obstructive jaundice;
- cirrhosis;
- psoriasis;
- Paget’s disease of bone;
- gastric bypass;
- obesity.

Limitations:
For Medicare beneficiaries, screening tests are governed by statute (Social Security Act 1861 {nn}). Vitamin D

testing may not be used for routine screening.

Assays of calcitriol need not be performed for each of the above conditions. The most common type of vitamin D deficiency is that of 25 OH Vitamin D.

The 1,25-dihydroxy form of vitamin D is generally only required to assist in the diagnosis of certain cases of rare endocrine disorders (primary hyperparathyroidism, hypothyroidism, pseudohypoparathyroidism), or for diagnosing and treating renal osteodystrophy and vitamin D-dependent and vitamin D resistant rickets, or in cases of unknown causes of hypercalcemia, including sarcoidosis. Level of both 25OHD and calcitriol are not needed as a panel for determining a patient's vitamin D status or to monitor routine vitamin D replacement therapy for most diseases. It is expected that the medical record will justify the tests chosen for a particular disease entity, that all available components of 25 OH vitamin D and other metabolite levels will not be performed routinely on every patient and that supportive documentation for test choices will be available to the Contractor upon request.

This Contractor does not expect to receive billing for the various component sources of 25 OH vitamin D separately (such as stored D or diet derived D). Only one total 25 OH vitamin D assay (comprising the sum of both 25OHD2 and 25OHD3) will be considered for reimbursement on any particular day, if medically necessary, for the patient's condition.

Once a beneficiary has been shown to be vitamin D deficient, further testing may be medically necessary only to ensure adequate replacement has been accomplished for this vitamin deficiency, although, generally, other parameters are measured. Annual testing of the vitamin D status may be appropriate depending upon the indication and other mitigating factors. Because there can be variability in individual 25OHD responses to supplemental vitamin D in high-risk individuals, the serum 25OHD levels could be retested after about 3 months of supplementation to confirm that the target 25OHD level has been reached. If the follow up test shows they have not yet reached the target level, the test can it be repeated in another 3 months until the target level is achieved.

Testing Methods
Several methods are available for measuring circulating concentrations of 25-OH-D. Medicare will cover laboratory tests that give practitioners accurate and reliable information. The method used to perform this testing should be validated.

Summary of Evidence

N/A

Analysis of Evidence
(Rationale for Determination)

N/A

General Information

Associated Information

Documentation Requirements
The patient's medical record must contain documentation that fully supports the medical necessity for services included within this LCD. (See "Coverage Indications, Limitations, and/or Medical Necessity.") This documentation includes, but is not limited to, relevant medical history, physical examination, and results of pertinent diagnostic tests or procedures.

Utilization Guidelines
In accordance with CMS Ruling 95-1 (V. Acceptable Standards of Practice - - Application), utilization of these services should be consistent with locally acceptable standards of practice.

1. Only one 25 OH vitamin D level will be reimbursed in any 24 hour period. Storage and supplement components will not be reimbursed separately.
2. Only one 1,25-OH vitamin D level will be reimbursed in a 24 hour period if medically necessary.
3. Assays of vitamin D levels for conditions other than for Rickets, vitamin D deficiency, osteomalacia, and aluminum bone disease will be limited to once a year.
4. Assays of the appropriate vitamin D levels for Rickets, vitamin D deficiency, osteomalacia, and aluminum bone disease will be limited to 4 per year, for the previously identified deficient form of vitamin D.
   (Because there can be variability in individual 25OHD responses to supplemental vitamin D in high-risk individuals, the serum 25OHD levels could be retested after about 3 months of supplementation to confirm that the target 25OHD level has been reached. If the follow up test shows they have not yet reached the target level, the test can be repeated in another 3 months until the target level is achieved.)

Sources of Information

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Bibliography

N/A

Revision History Information

REVISION HISTORY DATE	REVISION HISTORY NUMBER	REVISION HISTORY EXPLANATION	REASON(S) FOR CHANGE
10/31/2019	R12	10/31/2019 Change Request 10901 Local Coverage Determinations (LCDs): it will no longer be appropriate to include Current Procedure Terminology (CPT)/Health Care Procedure Coding System (HCPCS) codes or International Classification of Diseases Tenth Revision-Clinical Modification (ICD-10-CM) codes in the LCDs. All CPT/HCPCS, ICD-10 codes, and Billing and Coding Guidelines have been removed from this LCD and placed in Billing and Coding: Vitamin D Assay Testing linked to this LCD. Consistent with Change Request 10901 language from IOMs and/or regulations has been removed and the applicable manual/regulation has been referenced.	• Other (Changes in response to CMS Change Request 10901)
10/01/2019	R11	09/26/2019: Group 1 Codes: removed Z68.30-Z68.45 from code range and listed individually. ICD-10 CM code annual update in Group 1 Codes: Z68.43 description change. Review completed 09/03/2019.	• Revisions Due To ICD-10-CM Code Changes • Other ((Annual Review))
10/01/2018	R10	10/01/2018 Annual review done 08/31/2018. ICD-10 code updates: description change to code Z68.43; deleted codes K83.0 and M79.1; and added codes K82.A1, K82.A2, K83.01, K83.09, M79.10, M79.11, M79.12, and M79.18.	• Revisions Due To ICD-10-CM Code Changes • Other (Annual Review)
10/01/2017	R9	10/01/2017 Annual review done 09/02/2017. Per ICD-10 code updates: To Group 1 description changes to codes M33.01, M33.02, M33.09, M33.11, M33.12, and M33.19; and added codes M3303, M33.13, and M33.93.	• Revisions Due To ICD-10-CM Code Changes • Other (Annual Review)
09/01/2017	R8	09/01/2017: Added the following codes to Group 1 for 82306: B38.0-B38.89, B39.0-B39.5, C82.00-C82.99, J63.2, M80.00XA-M80.88XS, Z68.30-Z68.45, and Z98.0. Added "obesity" to the list of indications for the measurement of vitamin D levels in the narrative section. At this time 21st Century Cures Act will apply to new and revised LCDs that restrict coverage which requires comment and notice. This revision is not a restriction to the coverage determination; and, therefore not all the fields included on the LCD are applicable as noted in this policy.	• Revisions Due To ICD-10-CM Code Changes

REVISION HISTORY DATE	REVISION HISTORY NUMBER	REVISION HISTORY EXPLANATION	REASON(S) FOR CHANGE
10/01/2016	R7	10/01/2016 Annual review done. Per ICD-10 Code Updates: in Group 1 deleted codes K85.1, K86.8, and K90.4 and added codes K85.10, K85.11, K85.12, K86.81, K86.89, K90.41, and K90.49, effective 10/01/2016.	• Other (Annual Review) • Revisions Due To ICD-10-CM Code Changes
10/01/2015	R6	12/01/2015 Added codes C22.0, C22.1, C22.2, C22.3, C22.4, C22.7, C22.8, C22.9, C23, C24.0, C24.1, C24.8, C24.9, C25.0, C25.1, C25.2, C25.3, C25.4, C25.7, C25.8, C25.9, C26.0, C26.1, C26.9, D13.0, D13.1, D13.2, D13.30, D13.39, D13.4, D13.5, D13.6, D13.7, D13.9, K80.01, K80.11, K80.13, K80.19, K80.21, K80.31, K80.33, K80.35, K80.37, K80.41, K80.43, K80.45, K80.47. K80.51, K80.61, K80.63, K80.65, K80.67, K80.71, K80.81, K82.0, K82.8, K82.9, K83.0, K83.1, K83.2, K83.3, K83.4, K83.5, K83.8, K83.9, K85.1, K86.2, K86.3, K86.8, K86.9, K87, M85.80, M85.811, M85.812, M85.821, M85.822, M85.831, M85.832, M85.841, M85.842, M85.851, M85.852, M85.861, M85.862, M85.871, M85.872, M85.88, and M85.89 to Group 1 table with an effective date of 10/01/2015. Removed CAC information. Formatting changes made.	• Other (ICD-10 Code Update) • Revisions Due To ICD-10-CM Code Changes
10/01/2015	R5	10/06/2015 - Due to CMS guidance, we have removed the Jurisdiction 8 Notice and corresponding table from the CMS National Coverage Policy section. No other changes to policy or coverage.	• Other
10/01/2015	R4	10/01/2015 Annual review done. Formatting changes made. Updated Sources of Information. No change in coverage.	• Other (Annual review)
10/01/2015	R3	10/01/2014: Annual review done 09/09/2014. Formatting and punctuation changes made. Sources of Information updated. No change in coverage.	• Other
10/01/2015	R2	07/01/2014 For clarity, added the ICD-10 codes for vitamin D deficiency E55.0, E55.9, E64.3, M83.0 – M83.5, and M83.8 – M83.9 under the utilization guidelines. Theses codes already appear in the chart of Group 2 codes. No change in coverage.	• Other
10/01/2015	R1	04/01/2014 Removed reference to ICD-9 and changed to ICD-10. No change in coverage.	• Typographical Error

Associated Documents

Attachments

N/A

Related Local Coverage Documents

Article(s)
A57484 - Billing and Coding: Vitamin D Assay Testing

Related National Coverage Documents

N/A

Public Version(s)

Updated on 10/23/2019 with effective dates 10/31/2019 - N/A
Updated on 09/17/2019 with effective dates 10/01/2019 - 10/30/2019
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Some older versions have been archived. Please visit the MCD Archive Site to retrieve them.

Keywords

N/A